

Population Pressure Diluted

THE British government's population panel, under the chairmanship of Professor C. R. Ross of the Central Policy Review Staff, has produced an exhaustive report of the possible effects of different levels of population in Britain in the next hundred years (*Report of the Population Panel*, HMSO, Cmnd. 5258, £0.90). It is at once clear that the panel's recommendations are well founded and that its approach to assessing whether or not Britain should have a population policy can be commended. In particular, the presentation to government departments of three alternative models of the British population for fifteen and forty years ahead when asking these departments for their views on the relevance of population trends was a wise move, the success of which will benefit other inquirers of these departments.

But what of the recommendations? The panel suggests that the government should not in future regard the level and rate of increase of the population with indifference but also, quite properly, it does not see the need for fiscal policy to influence the size of families in the foreseeable future. But the panel is loud in its warning that the government should not have a population policy that sets a definite limit for the British population at some time in the future. It is proper that the panel has steered clear of defining an optimum population, for there are no accurate ways of calculating this figure in terms of economic benefits to the country, but suggestions which have been made that the optimum British population should be 30 million, based presumably on the fact that only enough food is produced within Britain to feed this number, are quite sensibly dismissed by the panel on the grounds that "to frame policy in terms of 'targets' which take no account of the built-in momentum of the demographic process or the uncertainties about the extent to which population growth can be influenced by policy is neither sensible nor realistic".

It now seems that the population of Britain will increase from its present value of about 55 million to 64 million sometime during the first decade of the next century. It is brave of the panel, in view of the concern that has been expressed about the size of the British population, to come out and say that given a not too unstable world situation, Britain should be able to find means of accommodating any likely increase in population over the next forty years. There will also be little disagreement with the panel's view that Britain would be better off with a stationary population than with an expanding one, although such a situation is unlikely to occur in the near future. For those that take apparent delight in predicting that catastrophe of one sort or another is around the corner, the report brings little comfort. Professor Ross is quite clear in his recommendation that provided the rate of increase of population does not change suddenly the prospects for the next thirty or forty years are such that no drastic action is required.

Much of the uncertainty and confusion which has arisen in the past about the implications of population growth has been caused by a palpable shortage of

information. Why do fertility rates change with no apparent rhyme or reason, the increase in Britain in the early 1960s in particular? Similarly, what are the factors which affect mortality, especially in children? To what extent do emigration and immigration affect population estimates? And with Britain now firmly entrenched within the European Economic Community the question has to be asked whether British people are going to move to Europe in increasing numbers or whether the Europeans will find the grass greener in Britain than in their homelands? The Population Panel has been equal to the challenge and the recommendation that a centre be set up for population studies is to be welcomed as indeed is the suggestion that it should be built at a university and that it should be closely connected to the economics, social sciences, biology and medical departments of that university.

Population, according to the panel, should become the responsibility of a senior non-departmental minister and a small group on population matters should be set up within the Cabinet Office together with an interdepartmental committee to coordinate all work on population. It is also recommended that the Office of Population Censuses and Surveys should also be expanded and strengthened, chiefly in order to analyse demographic data but also to commission research on population matters. A Minister for Population, as is admitted in the report, could not be effective without having at his fingertips a great deal more information on population than is now available. This, combined with the panel's assurance that the expected increase in the British population in the next thirty or forty years is not likely to cause difficulties, makes the need for a minister less immediate than the need for more research in demography.

Tunnelling for Trouble

THE British and French governments, having apparently learned nothing from their ill-starred Concorde project, seem bent on spanning the English Channel with a tunnel first proposed in the 1850s and which is unlikely now to be an economic proposition. In a memorandum on the subject published last week (*The Channel Tunnel Project*, Cmnd 5256, HMSO, £0.365), the Minister for Transport Industries, Mr John Peyton, says, to be sure, that "the project will only be undertaken if it is shown by the current technical, economic and financial studies to be a sound business proposition" but he has also spelled out a timetable for making a decision which is exceedingly tight. The document says that a treaty between France and the United Kingdom will be needed by July 31 this year and that preliminary works on the tunnel would begin this autumn with the prospect of a final agreement on the financing of the tunnel itself being signed early in 1975, just two years from now. There is no objection to the way in which the project has several intermediate decision points, but it is seriously to be questioned



whether an objective view of the economics of the tunnel could be formed in the next three months. Certainly it is hard to see why there should be such a rush to begin work on a project which is likely to cost far in excess of the figure of £366 million now quoted for the tunnel, and which is itself innocent of the not inconsiderable interest charges that would accrue in the next decade.

The objections to the tunnel project mount as the months go by. It is true, of course, that traffic between Britain and the mainland is increasing rapidly. The government document calculates that traffic of most kinds is now doubling every decade. The big uncertainty in the plan for a Channel tunnel is the extent to which enough of this increase could be attracted to the tunnel. No doubt the government is right to calculate that a through train service between London and Paris could put the airlines now operating on that route at a disadvantage, and it is also true that increasing congestion at Channel ports in the summer may persuade holiday makers that it would be better to put their cars on a train and make the journey across the water in relative comfort. But this business is unlikely by itself to make the Channel tunnel profitable. What really matters is what the future pattern of freight traffic will be, and whether the comparatively high yielding passenger traffic between Britain and the mainland, as distinct from the traffic between Dover and Calais, can be persuaded into the tunnel. The prices now being offered by Channel ferry operators are already competitive with those likely to have to be charged to make the tunnel profitable, there are difficulties in using continental freight cars and passenger carriages on British railways and the government's calculation of the cost of the tunnel leaves out of account the need to build new access roads to the coast of Kent so as to service the tunnel terminals. The biggest danger in the government's commitment to the Channel tunnel is that it may find itself, several years from now, controlling the competition across the Channel so as to create an artificial demand for the service it now proposes to provide.

What can be done by other means to accommodate the growing demand for cross-Channel travel? This is what the two governments should urgently be asking themselves in the weeks ahead. So far as passengers are concerned, there is plenty of scope for making the present system more efficient by improving the facilities for air travel which at present exist. Why is there, for example, no air shuttle service between London and Paris? Why are air fares so high and seats on aircraft so hard to buy? Where other kinds of travel are concerned, the government should recognize that there is a need for travel between Britain and the Low Countries, with Germany beyond, which is unlikely to be satisfied easily by a narrow link between Kent and the Pas de Calais. At least one sensible alternative to the Channel tunnel which should now be considered is the establishment of one or two substantial new ports on the east coast of Britain. The growth of East Anglian ports in the past few years shows where this demand applies. It might now be sensible to think of further developments along these lines, either on the Thames estuary or even on that never-never bit of Britain—the Goodwin Sands—which might provide sea links in their way as efficient as the tunnel now proposed.

In the long run, however, the government should pay more attention than it has to the possibility of forging a

surface link between Britain and the continent. One possibility, lightheartedly dismissed in the document now published, is that there should be a bridge. Another is that deliberate attempts should be made to shorten the sea-link between Britain and the continent by means of barrages, land reclamation projects and the like. Although the government has often mentioned possibilities like these, it has never given them the serious consideration they deserve. The danger now is that it will be hustled into a rapid decision on the Channel tunnel without taking account of the effects that such a link will have on the whole pattern of transport between Britain and the rest of Europe.

100 Years Ago



With regard to the question of the means by which animals find their way home from a long distance, a striking account, in relation to man, will be found in the English translation of the Expedition to North Siberia, by Von Wrangell. He there describes the wonderful manner in which the natives kept a true course towards a particular spot, whilst passing for a long distance through hummocky ice, with incessant changes of direction, and with no guide in the heavens or on the frozen sea. He states (but I quote only from memory of many years standing) that he, an experienced surveyor, and using a compass, failed to do that which these savages easily effected. Yet no one will suppose that they possessed any special sense which is quite absent in us. We must bear in mind that neither a compass, nor the north star, nor any other such sign, suffices to guide a man to a particular spot through an intricate country, or through hummocky ice, when many deviations from a straight course are inevitable, unless the deviations are allowed for, or a sort of "dead reckoning" is kept. All men are able to do this in a greater or less degree, and the natives of Siberia apparently to a wonderful extent, though probably in an unconscious manner. This is effected chiefly, no doubt, by eyesight, but partly, perhaps, by the sense of muscular movement, in the same manner as a man with his eyes blinded can proceed (and some men much better than others) for a short distance in a nearly straight line, or turn at right angles, or back again. The manner in which the sense of direction is sometimes suddenly disarranged in very old and feeble persons, and the feeling of strong distress which, as I know, has been experienced by persons when they have suddenly found out that they have been proceeding in a wholly unexpected and wrong direction, leads to the suspicion that some part of the brain is specialised for the function of direction. Whether animals may not possess the faculty of keeping a dead reckoning of their course in a much more perfect degree than can man; or whether this faculty may not come into play on the commencement of a journey when an animal is shut up in a basket, I will not attempt to discuss, as I have not sufficient data.

CHARLES DARWIN

From Nature, 7, 418, April 3, 1873

OLD WORLD

Nuclear Power: Weinstock at the Helm

BRITAIN'S nuclear design and construction industry has finally been restructured with Sir Arnold Weinstock ultimately in charge.

Under the government's proposals, a new company is to be formed, 50 per cent of which will be owned by Sir Arnold Weinstock's General Electric Company, 35 per cent by a shareholding company into which other members of Britain's existing nuclear power industry can buy, and 15 per cent by the government held through the United Kingdom Atomic Energy Authority.

It is clear where the power is to lie. Mr. Peter Walker, Secretary of State for Trade and Industry, announcing the government's decision in the House of Commons last week said that GEC will "also play a supervisory role on a basis agreed with the main board of the new company". GEC will be paid for its services.

This arrangement is different in name from that which the government considered earlier this year when there was talk of awarding a management contract to someone like GEC. It is, however, unlikely to prove different in practice. Mr Tom Boardman, giving evidence to the Select Committee on Science and Technology this week, made it plain that GEC will provide the management of the new company which is to have a two tier structure. The chief board will be appointed jointly by GEC and the government. It in turn will appoint a managing board to actually run the new company.

The new £10 million organization will be chaired by Lord Aldington, GEC's deputy chairman, with Lord McFadden, currently chairman of British Insulated Callendar's Cables as deputy chairman. A chief executive has yet to be appointed. Although existing companies in the nuclear design and construction industry can buy into the shareholding company that, with GEC and the government, will own the new company, they will not be able to directly influence the management.

This reorganization, which follows the announcement made last August that the nuclear power industry was to be concentrated in one bloc, is the first stage in ending the uncertainty that has hung over the industry for the past two years. Later this month Mr Walker is expected to announce the membership of the Nuclear Power Board which will advise him on the choice of reactor system. Its membership is expected to

include representatives from the UKAEA, the Central Electricity Generating Board, the Electricity Council and government scientists.

Mr Walker told the Commons that the consultations that have taken place over



Sir Arnold Weinstock

the past six months "have confirmed strongly the government's view that there should be a single nuclear company which will use the skills and experience of the existing industry".

The radical differences between the new company and the old consortia (British Nuclear Design and Construction and The Nuclear Power Group) will be that the new company will have

a single strong management, and will be responsible only for the design and construction of the nuclear steam supply systems—in other words the reactor itself. Turbogenerators and other plant will be supplied by other contractors.

Although the government will only have a 15 per cent holding in the new company it will retain "special rights in certain matters where the public interest is closely involved", Mr Walker said. "These would include the formation of international links and securing that an open purchasing policy is pursued in order that neither the company's shareholders nor GEC subsidiaries should obtain preferential treatment."

The existing work of the nuclear consortia will be taken over by the new company "under arrangements to be agreed". The position of British Nuclear Fuels in the new set up is not entirely clear. Mr. Walker said that the fuel company "will be closely associated with the new company in marketing and exploiting reactor systems and their fuel", but its precise relationship has not yet been defined. Mr Boardman told the select committee that a joint marketing company may be formed by BNFL and the new company.

Although the new organization is expected to begin operations soon, and although the Nuclear Power Board should convene and produce its advice for Mr Walker comparatively quickly, new nuclear power station orders are unlikely before next year.

US/USSR

All Aboard the Glomar

THE Soviet Union is to collaborate with the United States in a deep sea drilling project using the Glomar Challenger. This latest development in Soviet-United States cooperation follows last May's open ended agreement on scientific cooperation (see also page 294).

The Soviet Union has been interested in sea bed exploration for some time, and the current five-year plan (see *Pravda*, February 14, 1971) provides support for such projects. Until now, however, these have only involved off-shore exploration for oil and minerals in the Caspian and Black Seas and on the eastern coast of the Soviet Union.

Under the new agreement the Soviet Union will contribute \$1 million a year (ten per cent of the total cost) to the Deep Sea Drilling Project, and Soviet

scientists will have facilities for further research work carried out by the Glomar Challenger.

To date the Deep Sea Drilling Project has been based on JOIDES, a consortium of five United States oceanographic institutions. Under the new agreement the Institute of Oceanology of the Soviet Academy of Sciences will represent the Soviet Union as the sixth member of the consortium.

Although new collaborative projects are planned under last May's agreement, some of which, for example, the Bering Meteorological project (see *Nature*, 241, 420; 1973) have already taken place, this entry of the Soviet Union into existing United States work seems an unprecedented move by the Soviet planners. Soviet scientists have, however, shown considerable interest in the voyages of the Glomar Challenger for some time, and regular reports of her movements and findings have appeared in *Priroda*.

POPULATION

Government Involvement

GOVERNMENTS can not afford to dissociate themselves from population questions, according to the *Report of the Population Panel* published last week (HMSO, Cmd 5258, 90p). The panel adds that "public opinion demands, and the facts of the population situation require, that the Government defines its attitude to questions concerning the level and rate of increase of population". The government should also, says the panel, indicate the extent to which population issues influence its policies and its choice of priorities.

By coming out in favour of the government being involved in population matters the panel echoes the sentiments of the Select Committee on Science and Technology which produced a report on population in 1971 that was the starting point for the present report.

But the panel reports that a "population policy is not a panacea for curing the ills of contemporary society". Those who suggest this, says the panel, are diverting attention from serious problems and the action needed to tackle them. The panel points out that "pressure on the countryside, congestion, social tensions, individual stress and alienation" will be serious problems whether the population of Britain is 55 million, as at present, or 70 million, which according to the latest report of the Government Actuary (see *Nature*, 240, 173; 1972) it is not now likely to be before the middle of the twenty-first century.

Population affairs should be a ministerial responsibility, says the panel, but there is insufficient knowledge of population trends and their causes and implications for a population policy to be formulated at present. To provide more information the panel recommends that a census be carried out in 1976, five years before the next planned one, and that censuses in future should be held regularly once every five years.

To provide more demographic information the panel recommends that a centre for population studies be set up at a university. The centre should be closely allied with other departments—economics, social sciences, biology and medicine being the ones specifically mentioned.

One of the great barriers to making accurate estimates of population is a lack of knowledge of how fertility rates change. In particular there is little knowledge of how fertility varies with social class and with where the mother lives in Britain. The panel calls for research in this area and it also points out that the effects of divorce and re-

marriage on fertility are little understood.

There has also not been anything approaching a national survey on the effectiveness of contraceptive techniques although the work by the Universities of Hull and York in the city of Hull is well known. There is also a need for more research into the relationship of abortion and sterilization to fertility.

The second area, which the panel pinpoints as being in need of research is mortality and it points out that the factors affecting the death rate are largely unknown, especially for children. There is also little knowledge of why the death rate in Britain changes from region to region. There is a need for more information on the death rate simply so that more accurate predictions of the age structure of the population can be made.

The panel also says that there is need for research into the effects of both emigration and immigration, especially now that entry to the European Economic Community has, in principle, made it easier for Europeans to live in Britain and for the British to live in Europe.

The panel also points to the need for correlating fertility with IQ and other variables for which suitable tests exist or can be developed. Such tests should be carried out at regular intervals in order to detect trends.

To coordinate research and information on population, and also to provide information for the minister, the panel recommends that a small group be set up in the Cabinet Office to advise on population matters and that a committee be set up of representatives from all government departments under the chairmanship of the head of the Cabinet Office group. The terms of reference of the group would require it to determine priorities within the population field.

As a further boost to demographic research the panel recommends that the Office of Population Censuses and Surveys should be expanded and strengthened both for the analysis of demographic data from censuses and other sources and for survey work on motivation and family planning. OPCS should also commission research and should be the vehicle which disseminates information and interpretative comment on population trends.

Perhaps the recommendation of the panel which has caused most comment in the past week is that comprehensive family planning services should be provided as an integral part of the National Health Service "so that everyone knows of their existence and is free to use them". The government announced on Monday that contraceptives will be available to all on the same basis as drugs and appliances from April 1, 1974. In this respect contraceptives will not be

free—except for those that qualify for normal exemptions from prescription charges—and the estimated cost to the National Health Service will be £13 million, which is £3 million less than it would be if no charges are imposed.

CANCER RESEARCH

ICRF Spending Rises

EXPENDITURE by the Imperial Cancer Research Fund last year reached £2.7 million, £0.9 million of which went on capital developments at the fund's chief research centres at Lincoln's Inn Fields and Mill Hill (ICRF Annual Report).

The extension of the Lincoln's Inn Fields' building was finally completed late in 1972, a year behind schedule, providing the fund with an extra 41,000 square feet of space.

The year also saw the opening of the fund's medical oncology unit at St Bartholomew's Hospital with the intention of investigating how the various treatments for cancer, particularly chemotherapy and immunotherapy, can best be used, and discovering whether recent work on immunotherapy in animals can be applied to man.

The unit's current work includes attempts to lengthen periods of complete remission in patients with leukaemia and work on detecting relapses before they are clinically apparent.

The breast cancer unit at Guy's Hospital was closed last year, two years after it opened, in order to enlarge the two storey building by adding a floor; when the unit reopens in July 1973, 36 beds will be available instead of the original 21. The unit is also planning a large prospective cancer study on women in south east London. This follows the unit's study of 5,000 women in Guernsey which has been running since 1961 and has confirmed that abnormalities of androgen excretion are found in a high proportion of women who subsequently develop breast cancer. The unit is also comparing all aspects of breast cancer in Britain and Japan. This study, which is being carried out in collaboration with the National Cancer Centre, Tokyo, could produce some interesting results because breast cancer is very rare in Japan.

Clinical trials of ICRF 159, the drug that the fund has developed which appears to be effective against secondary tumours, have begun in the United States and in Britain, chiefly at Westminster Hospital. It is too early yet for any firm conclusions to be drawn as the trials have only been running for six months, but Dr Kurt Hellmann, head of the fund's chemotherapy unit, said this week that the first results "look very encouraging".

ICRF raised £1.7 million during 1972, an increase of £0.12 million over

1971. Of the £1.8 million current expenditure during the past year, £0.9 million was spent on research staff salaries, £130,000 on new equipment, and £214,000 on laboratory upkeep and materials.

ICELANDIC SCIENCE

Need for Expansion

ICELAND spends 0.39 per cent of its Gross National Product on research and development, a much smaller percentage than that in most other western countries, and the country's expenditure on research and development has only increased very slowly since 1950 when it ran at 0.17 per cent of the GNP (*Reviews of National Science Policy, Iceland, OECD, Paris*).

Research in Iceland is funded mostly by the government, which provides more than 70 per cent of the money, with industry running a poor second with 17 per cent of the research funding to its credit. In all, in 1971, 187.7 million Icelandic kroner (£79 million) was spent on research and development which was allocated as follows: Kr42.8 million on basic and unspecified research, Kr41.6 million on agricultural research, Kr67.4 million on fisheries research, Kr41.6 million on agricultural and construction, Kr24.3 million on energy research and Kr4.7 million on medical research. In 1966, by comparison, the total spent was Kr72.7 million and the greatest increase between 1966 and 1971 was in spending on fisheries research which went up from Kr20.6 million to Kr67.4 million.

The OECD examining team, consisting of Dr Alexander King, the Director General for Scientific Affairs at the OECD and Dr R. Major, the director of the Norwegian Council for Scientific and Industrial Research, has strong criticisms of the organization of research in Iceland. They say that the resources available for research are inadequate and that the absolute resources devoted to science "seems less than the critical amount necessary for a modern society".

Iceland has one university, and during 1970-71, 1,640 students were registered. But more than 700 Icelanders were studying abroad. Only 260 engineers and science students were registered at the University of Iceland in 1970-71 but a number of scientists were also studying abroad. Drs King and Major call for a further development of the Department of Technology and Science at the university which apart from redressing the balance of science students will form a nucleus for fundamental research "which should be oriented towards the specific natural conditions and national needs in Iceland". To overcome the difficulties of building up

this department it is suggested that the staff of the Icelandic applied research institutes be involved in teaching in the university.

The National Research Council of Iceland was formed in 1940 and is the only body in the country charged with handling scientific matters on a broad basis. Iceland has no minister for science, and scientific affairs are dealt with separately by each ministry. The National Research Council is, at present, attached to the Ministry of Education but the examiners suggest that the council should be attached in future to the Prime Minister's office and also that it should be considerably strengthened by altering its membership with a view to making it a more active organization. The NRC, say the examiners, should take the initiative to create strategies and long-range plans for research activities "harmonized to the national goals of the country".

The examiners also suggest that the Icelandic applied science institutes should continue to report to their ministries but that they should strengthen their contacts with the users of their work and they also recommend that industry should be encouraged to undertake research projects. Very little research is undertaken in industry at present and this is "in the long run an unhealthy situation".

But the final words of advice from Dr King and Dr Major are that, apart from insufficient resources, the "main obstacle to the progress in science in Iceland appears to be the lack of communication and open dialogue".

CIBA FOUNDATION

Fostering Relations

THE Ciba Foundation, which exists to promote international cooperation in medical and chemical research, spent £160,000 in 1972 and sponsored no fewer than thirteen symposia at its London headquarters in Portland Place, as well as holding several smaller meetings and discussions.

The foundation was set up in 1947 by CIBA Ltd and is now financed by that company's successor, CIBA-Geigy Ltd. Each year a third of the foundation's funds come from the parent company in Basle, a third from its subsidiary in Britain and a third from subsidiaries in the United States, Canada and Mexico among other countries.

Broadly speaking 50 per cent of the expenditure each year is for scientific purposes, 30 per cent for the maintenance of the "house"—in which, among other things, accommodation is provided free for scientists visiting Britain on business—and 20 per cent on administration. Although the lion's share of the scientific expenditure is on confer-

ences and so on, the foundation does spend on average about £1,200 a year on its Anglo-French medical exchange bursaries, which allow young French and English scientists to interchange countries for a month or two. The foundation's annual report published recently lists nine bursaries—eight to British scientists—for 1972-73.

The Ciba Foundation also spends about £500 a year on associateships at the Royal Society of Medicine; this allows about twenty foreign students a year to make use of the facilities of the society without becoming full members.

Among the symposia held by the foundation in 1972 were ones on locomotion of tissue cells, corneal graft failures, and the medical care and protection of prisoners and other detainees.

New job for Berrill?



SIR KENNETH BERRILL, chairman of the University Grants Committee, is being tipped to become the government's Chief Economic Adviser later this year in succession to Sir Donald MacDougall. The Treasury was unable to confirm this week that his appointment is imminent, but Sir Kenneth, who is a product of the London School of Economics and Trinity College, Cambridge, and who was a lecturer in economics at Cambridge from 1949-69, has both experience as a government adviser and a reputation as an extremely able administrator.

Sir Kenneth became Chairman of the University Grants Committee in 1969 and is due to retire this year; from 1967-69 he was special adviser to the Treasury, and he has also been an economic adviser to Turkey, British Guiana and the OECD.

NEW WORLD

Commission at Odds with Nixon's Drug Policy

by our Washington Correspondent

PRESIDENT NIXON was told last week that official responses to the problem of drug abuse in the United States have led to ill-defined but lavishly funded programmes, that a drug abuse/industrial complex has built up which has a vested interest in perpetuating the problem and that basic assumptions about the nature of drug abuse and its causes need to be reexamined. He was also again told that criminal sanctions against those who possess marihuana should be removed and that the rhetoric about drug abuse which constantly pours from government officials and legislators is counterproductive.

Such statements, not surprisingly, met with a cool reception from the White House, for only a week previously, President Nixon had been indulging in some high-flown rhetoric of his own, telling Congress that his Administration was making some progress in the fight against drug addiction, proposing fresh draconian legal sanctions against drug traffickers and restating his opposition to decriminalizing the use of marihuana.

The complaints about attitudes toward drug abuse and about responses to the problem came from the National Commission on Marihuana and Drug Abuse, a commission set up by Congress and charged with the task of examining the nature, causes and scope of drug abuse in the United States. If the commission's findings and recommendations are surprising, they are made even more so by the fact that nine of its thirteen members were appointed directly by President Nixon and that it was headed by Raymond P. Shafer, former Republican Governor of Pennsylvania, and not noted for liberal leanings. They were contained in the commission's second and final report, a long, closely argued document which opens up a window on the whole subject of the use and misuse of drugs and lets some welcome fresh air blow in.

The report* is an attempt to deflate emotions, cut through the rhetoric and examine the basic issues which surround drug abuse and its causes. Although the commission put forward some relatively far-reaching proposals, its chief effect will probably be to help provide an atmosphere in which official responses to drug use (the commission

cautions strongly against the use of words such as drug abuse and drug addiction) can be more rationally formulated. Its first report, which was published a year ago and which dealt just with the use of marihuana, similarly adopted a low-key approach, argued that the emotionalism surrounding the use of marihuana was partly responsible for its widespread use and recommended that criminal sanctions against the possession of small quantities of the drug should be removed.

The commission argues that although attention is usually focused on the opiates, and in particular on heroin, "alcohol dependence is without question the most serious drug problem" in the United States, and that addiction to

barbiturates is a more hidden problem, the dimensions of which are perhaps equivalent to the hidden opiate problem of the late nineteenth century. There are reckoned, for example, to be 9 million alcoholics in the United States. Society's attitudes towards the use of various drugs are, the commission suggests, inconsistent with respect to the costs of irresponsible use, both to society and to the individual.

Seen in terms of such costs, the commission suggests that social concern should concentrate on alcohol and heroin, that there should be moderate concern about the use of amphetamines, barbiturates, hallucinogens and cocaine and that marihuana and so-called minor tranquillizers merit the least social con-

JUPITER

Off to Jupiter Again

by our Washington Correspondent

THE second spacecraft to pay a visit to Jupiter, Pioneer G, will be launched from Cape Kennedy next week — weather and technical difficulties permitting. If all goes well it should reach Jupiter in December 1974, exactly a year after its predecessor, Pioneer 10, which was launched in March last year and which has now covered three quarters of the distance to the planet. Exactly what Pioneer G will do when it makes its rendezvous with Jupiter is still open to question, however, and will depend in large part on the results obtained by Pioneer 10.

One of the chief factors which will determine the nature of the mission is the intensity of the radiation trapped in belts around Jupiter. Some theories suggest that the intensity in the radiation belts may be about a million times stronger than in the Van Allen belts around the Earth, and it would destroy the instruments aboard a spacecraft which flies too close to Jupiter.

Before Pioneer 10 was launched, there was a strong argument for taking the spacecraft in as close to the surface as possible, so that the intensity of the radiation belts could be mapped, and so that data obtained from near the surface could be relayed back until the instruments ceased to function. It was finally decided, however, to take Pioneer 10 in to about three Jupiter radii from the centre of the planet, where the radiation should not endanger the spacecraft.

According to Mr. Charles F. Hall, the project manager, measurements taken by Pioneer 10 can be extrapolated to determine the radiation intensity closer to Jupiter, and a meeting of those who have experiments aboard Pioneer G will be called early next year to plan the mission in the light of those measurements. Mid-course corrections will then be made to the trajectory of Pioneer G (which will be renamed Pioneer 11 after launch) to alter its closeness of approach and its path past Jupiter. After the encounter with the planet, both spacecraft will eventually leave the solar system.

If the radiation intensity is not as great as some fear, and if there is sufficient thruster gas left on the spacecraft for mid-course corrections, the trajectory of Pioneer G could be altered so that it would swing past Jupiter at a distance of about half a Jupiter radius from the cloud tops, and go on to an encounter with Saturn in 1980. That would require the spacecraft to pass across the face of the planet, however, rather than behind it, and that would not be the best course from the point of view of some of the experiments. There is also a possibility of taking a look at some of the moons of Jupiter. Pioneer 10 will pass behind Io, for example, when it will be possible to tell from the effect on the radio signals whether the satellite has an atmosphere.

At least one uncertainty has been reduced by the data already sent back by Pioneer 10. The spacecraft recently completed passage through the asteroid belt and it found fewer large particles in the belt than most estimates predicted.

**Drug Abuse in America: Problem in Perspective*, available from the US Government Printing Office, Washington DC 20402, \$2.60. Stock No 5266-00003.

cern at present.

In short, the commission believes that society should adopt what can best be described as a public health policy towards the use of drugs. Arguing that the rationale behind federal, state and local programmes designed to prevent abuse and to treat and rehabilitate so-called drug abusers needs careful re-examination, the commission suggests that law enforcement, information and education, treatment and rehabilitation and scientific research all have important parts to play. But in each of these areas, present policies and attitudes leave much to be desired.

As for law enforcement, the commission believes that federal efforts, which are split between the Customs Bureau and a sheaf of agencies in the Department of Justice, are badly co-ordinated. It suggests also that a vigorous enforcement effort should be directed at middle and upper level traffickers, rather than at street level pushers, but argues strongly against minimum mandatory sentences. This is in sharp contradiction to proposals sent to Congress by President Nixon just a few days before the report was published. President Nixon called for jailing anybody convicted of selling small quantities opiates for 5 years, for a minimum of ten years in prison for those convicted of selling larger amounts, and for life imprisonment without parole for second offenders convicted of selling more than four ounces of an opiate. Mandatory minimum sentences, the commission believes, would be counter-productive, for in many cases judges may be more ready to acquit an offender rather than to lock him up and throw away the key.

The commission agonizes over the question of whether or not simple possession of an illegal drug should constitute a crime, and finally decides that only in the case of marihuana should criminal sanctions against possession be lifted. It comes to such a conclusion for two chief reasons. First, removal of criminal sanctions for possession of an illegal drug may also remove some discouragement of its use, and second, enforcement of the possession laws will help to detect persons who may benefit from treatment. Following from that, the commission recommends that a drug-dependent person arrested for an offence related to his dependence should be put into a treatment programme either in lieu of prosecution, or after conviction but before sentencing. Failure to comply with the conditions of treatment would result in return to court for conviction or for sentencing.

As for treatment, the commission believes that money has been poured into programmes with little evaluation of their effectiveness and concludes that "fundamental assumptions are not ques-

tioned, programs are not evaluated and the problem is perpetuated from fiscal year to fiscal year. 'Drug abuse' spending in the last decade can be summarized thus: an ill-defined problem emotionally expressed, led to ill-defined programs, lavishly funded."

On methadone maintenance for heroin-dependent persons, the commission suggests that it "is a promising means of neutralizing the opiate-dependent person's preoccupation with the drug. Provided drug-free regimens are also available as alternative treatment modalities, in every community, and voluntary entry is emphasized, we believe that treatment officials should continue to expand and improve maintenance services".

But the commission does decide to recommend against a heroin maintenance scheme such as the British method. If the objective is simply to reduce drug-related crime, then a heroin maintenance scheme would be appropriate, but the commission suggests that heroin maintenance schemes would tend to displace methadone maintenance, that the benefits to the dependent person are outweighed by the therapeutic disadvantages, and that in any case, other treatment methods have not yet been given a fair chance. Nevertheless, the

commission believes that the British heroin maintenance scheme should be carefully evaluated.

The report also has harsh words to say about drug information and education programmes, suggesting that they have not been properly evaluated, that many present factually incorrect material, and that some may even lead to increased use of dangerous drugs. The commission is consequently driven to recommend that an immediate moratorium be placed on the production and dissemination of new drug information materials until standards for accuracy and concept can be drawn up, and that in view of the ignorance about the impact of drug education, a moratorium should be placed on drug education programmes in schools. At the very least, the commission recommends that state laws requiring compulsory drug education classes in schools should be repealed.

Perhaps the commission's chief recommendation, directed at the federal government, is that a single, independent federal agency should be established, on the lines of the Atomic Energy Commission, to establish, coordinate and administer all government drug policy. The agency, which could be called the Controlled Substances

EARTHQUAKES

Quake-waiting

by our Washington Correspondent

THE first official prediction that an earthquake will take place at a specific location was made last week by the US Geological Survey. There is a "good likelihood", the survey said, that a small earthquake of magnitude about 4.5 and with a focal depth of about 3.5 miles will occur at a point on the San Andreas fault about 20 miles south-east of Hollister, a small town in northern California. The only parameter which cannot be predicted so precisely is the timing—the event is expected to occur "within the next few months". Officials in the Geological Survey are quick to point out, however, that a unique and well documented set of events has led to the prediction and that other regions of the fault may not be so predictable.

In short, the earthquake is expected to take place at 36°40'N and 121°17'NE, on a segment of the San Andreas Fault which has been extensively studied by seismologists from the USGS research centre at Menlo Park. Four earthquakes of magnitudes between 4.0 and 5.0 have taken place at opposite ends of a 12.5 mile section of the fault since December 1971—two at the northern and two at the southern end—and these have increased the strain at the centre

of the section. The strain would be relieved by an earthquake of magnitude about 4.5.

Chiefly the work of two USGS seismologists, Robert L. Wesson and William L. Ellsworth, the prediction is contained in a paper which will be delivered at the annual meeting of the American Geophysical Union in Washington DC in April. The Geological Survey, anxious to allay any fears that may have arisen in Hollister after the prediction was picked up by the press last week, rushed out an announcement.

Another paper by Wesson and Ellsworth to be delivered at the AGU meeting gives details of a study of several earthquakes which took place in California between 1952 and 1972. In every case, they found that the quake was preceded by great numbers of micro-earthquakes, and they suggest that such activity "is a necessary condition for the later occurrence of a moderate or larger earthquake in California".

One result of the public announcement of the prediction is that there will probably be a rush of seismologists to the area of the predicted earthquake, and the event, if it takes place, will be very carefully studied. In particular, any precursors will be closely monitored, and much valuable data could result. If it does not occur, at least the USGS has the letout that it did not predict the time of occurrence.

Agency, would absorb the functions of agencies concerned with drug abuse law enforcement, treatment and rehabilitation, research and education. To avoid institutionalizing the drug problem, the commission also recommends that the agency should be disbanded after five years. Such a drastic step is recommended because there is considerable duplication between the various agencies and little effective coordination.

Last year a Special Action Office for Drug Abuse Prevention (SAODAP) was established in the White House to oversee and coordinate the work of the various agencies concerned with treatment, rehabilitation and education programmes. But the commission suggests that the office is at best a stop-gap measure, and it has failed to provide adequate coordination. And, on the law enforcement side, the report gives details of overlap, rivalry and lack of cooperation between the various drug abuse law enforcement agencies.

The Controlled Substances Agency would distribute and monitor grants to states for treatment, rehabilitation, prevention, education and law enforcement programmes, it would develop and implement a general research plan, it would evaluate ongoing programmes and it would provide a data bank for policy planning. Like the AEC, the head of the agency would be a sub-cabinet official who would report directly to the President.

But the proposal has little chance of being adopted. For one thing, Senator Jacob Javits and Senator Harold Hughes, the two Senate appointees on the commission, both dissented from the recommendation because they believe that the Special Action Office has not yet been given a chance to show its mettle. Their lack of support probably precludes passage of legislation by Congress to set up such an agency. More important, a few hours after the commission's report was made public, a White House press spokesman announced that President Nixon will soon send Congress a reorganization plan to amalgamate all the drug abuse law enforcement agencies into a single agency within the Department of Justice. Although that would fit in with the commission's desire to coordinate law enforcement activities, it leaves aside the treatment, information and research activities. But the reorganization would neatly cut the ground from under the commission's feet.

In sum, the commission's report is likely to find that its chief impact will stem not from its recommendations but from its appeal for a more rational approach from its low-key assessments of prevailing attitudes as well as from the emergence of such radical suggestions from such a relatively conservative body.

INTERNATIONAL COOPERATION

Cooperation Begins

by our Washington Correspondent

COOPERATION between the United States and the Soviet Union on a number of scientific projects, promised in an agreement signed during President Nixon's visit to Moscow nearly a year ago, finally got under way last week. The US-USSR Joint Commission on Scientific and Technical Cooperation, set up by the Moscow agreement (see *Nature*, 237, 247; 1972), held its first meeting in Washington and approved about twenty-five specific joint projects. Although the projects nearly all involve applied science and will ultimately be of benefit to industry, many of them will be carried out in universities. Approval was also given for Soviet participation in the US Deep Sea drilling Project (see page 289).

In addition to approving projects, the Joint Commission also designated specific individuals in each country to organize and coordinate the work involved in each project; and drew up guidelines for financing them. No funding levels have, however, been proposed.

In addition to the general agreement on scientific and technical cooperation, agreements on health research, environmental science and space research were also signed in Moscow last May. These other specific agreements have already produced results—putative human cancer viruses and drugs have been exchanged, a list of projects in environmental science has been agreed to, planning is progressing well on the joint Apollo-Soyuz docking mission and there has been much East-West travel by scientists and officials. And now that the Joint Commission has finally met—its first meeting has been put back several times since it was first due to take place last October—it is hoped that this new scientific detente will be extended to cover a number of new areas.

The commission agreed to proposals for joint research and development in six chief areas: energy research and development, application of computers to management, agricultural research, microbiological synthesis, chemical catalysis and water resources. The industrial bent of most of the projects is evident from the following examples in each area:

- In energy research, the commission decided to concentrate on five areas—electric power systems and transmission lines, including superconducting transmission, magnetohydrodynamics and solar and geothermal energy. Last year, when the agreement was first signed, thermonuclear research was widely canvassed as a possibility for joint coopera-

tion, but has since been dropped, possibly for security reasons.

- Systems analysis, the use of computers for managing large cities, econometric modelling and the design of software were agreed to as projects for cooperation in the field of the application of computers to management. Dr H. Guyford Stever, director of the National Science Foundation and the US co-chairman of the commission, said last week that strategic products which are embargoed for export from the United States to the Soviet Union, which includes computers, were not discussed.

- In agricultural research, crop breeding and protection, increased production of farm animals and poultry and the mechanization of agricultural production were agreed as priority areas.

- On water resources, the commission approved four projects for immediate implementation—water resource planning, cold weather construction techniques, automation and remote control of water resource systems, and the use of plastics in construction.

- In the area of chemical catalysis, the commission approved five projects, including the application of catalysis to life support systems for possible use in space exploration and the use of catalysis for environment control—the use of catalytic converters for reducing harmful emissions from automobile exhausts, for example.

- Finally, on microbiological synthesis, the commission decided that a group of scientists from the United States should visit the Soviet Union before priority areas were defined.

Short Notes

Honing the Knife

ALTHOUGH Senator William Proxmire's views on economy in federal spending are by now well known, his utterances on the space budget bear especially close watching this year because he has recently been made chairman of the Appropriations subcommittee which deals with NASA's budget. Proxmire has now suggested that the agency's proposed budget for 1974 should be cut by a further \$500 million, chiefly by scrapping the shuttle and stretching out the Skylab programme. The suggestion formed part of a counter-budget in which Proxmire outlined reductions of more than \$4,000 million in President Nixon's spending proposals for 1974, chiefly by taking the axe to several programmes of the Department of Defense. Apart from the shuttle and Skylab, Proxmire suggests that "additional savings could be made in a much more vigorous effort to substitute unmanned for manned space efforts".

NEWS AND VIEWS

Global Perspectives on Climate

THE realization during the first four decades of this century that global climates are subject to change has been followed by a large and increasing scientific activity aimed at describing the magnitude and extent of these changes. Coupled with this, the early interest shown in the subject by planners in agriculture, industry and government has developed into an outright demand that climatic forecasts be made a few years or even decades ahead. Any attempt at prediction based solely on local climatic experience will, however, tend to founder, for the underlying secular patterns of global climatic change have a tendency to affect local climate in a radical and unpredictable way, often altering the local climate beyond past experience.

During the past twenty years these essential global patterns of climatic variation have been emerging with increasing clarity from a large accumulation of local climatic records. It is now fairly well established that from the eighteenth century until the 1920s the global atmospheric circulation, including the principal momentum-carrying winds of both hemispheres, showed a remarkably uniform tendency towards intensification; as Mitchell and others have shown, this was accompanied by a warming of the global atmosphere, especially at high latitudes (*Proc. Rome Symp., Changes of Climate* (UNESCO and WMO), 161; UNESCO, Paris, 1963). There is some evidence for attributing this to an increase in the effective supply of solar energy, partly through an increase in the strength of the direct solar beam and partly through a reduction in the amount of volcanic dust in the stratosphere from the 1820s onwards. Early records of cyclone and anticyclone tracks in the Atlantic sector of the Northern Hemisphere suggest that this strengthening circulation was also accompanied by a contraction of the circumpolar vortex, a poleward shift of the axes of zonal winds and pressure belts and a lengthening of wavelengths in the upper westerlies. By the early 1930s, the Iceland Low lay further north on average than at any other time in this century and the more frequent invasion of the Arctic by depressions is held at least partly responsible for the well-known retreat of Arctic Sea ice during the 1920s and 1930s. Since then (more especially since the 1940s) this situation has been reversed with remarkable suddenness. A rapid decrease in atmospheric vigour has been accompanied by a cooling of the global atmosphere, a retraction of winds and pressure belts towards the equator, a decrease of wavelengths in the upper westerlies (at least in the Northern Hemisphere) and a record southward advance of sea ice in the European sub-Arctic. Perhaps the most plausible basic explanation is an apparent decrease in the intensity of the solar beam since the 1940s, which has been noted by several climatologists.

Whether or not the causes of these important climatic events have been correctly identified, their fundamental economic and social effects have become abundantly clear. During the present period of meridional global circulation the specific tendency over the European Arctic and sub-Arctic seas has been towards northerly meridionality and climatic deterioration. To give

examples from this small sector alone, the increased northerly airflow has been held responsible directly or indirectly for the extension of sea ice to the north Icelandic coast, for a drastic and economically important alteration in the annual spawning migration of the Atlanto-Scandian herring stock to Iceland and for delaying the spring production of phytoplankton in the southern Norwegian Sea. Further, Lamb (*Nature*, **223**, 1209; 1969) has noted a two-week shortening of the average growing season in England since 1950, compared with the warmest decades of this century. Such fundamental changes could also be described for other sectors of the hemisphere, notably those areas where an expanding population is extending agriculture to marginal lands.

The full recognition of the economic importance of these changes together with the realization of man's increasing ability to modify climate himself (whether knowingly or unknowingly) have given the chief impetus to the present search for the tendencies, causes and global interconnexions of prominent climatic events. Observational techniques, computer technology and model making of the whole atmosphere-ocean system have advanced to support this search. From the outset, however, it is apparent that the course of this research must, at least for the present, be governed by the virtual impossibility of producing true forecasts of long-term climatic events which may be acyclic in character and may last so long that there are no analogues within the short time span covered by climatic records. A more fruitful approach lies, first, in the use of powerful modern techniques of observation and analysis to monitor the principal climatic events as they occur and, second, in the determination of the likely cause and effect relationships that will follow the establishment of a given large-scale climatic anomaly. The work of Starr and Oort described on page 310 of this issue of *Nature* represents the former category of research, set against and confirming the known tendencies of global climate and providing an insight into the type of analysis which will be some day routine. The novelty of their approach lies in the remarkable scale of the work involved. From the General Circulation Library of the Massachusetts Institute of Technology, some 150 to 200 thousand individual observations were integrated to produce each of the sixty monthly mean values which describe the temperature of the bulk (92 per cent) of the atmospheric mass in the Northern Hemisphere between 1958 and 1963. The mean water vapour content of the same atmospheric mass was computed for the same period. The downward trends which are shown in the temperature and humidity of the hemisphere are unequivocal but are, as the authors admit, so steep as to make a long continuation of the trend seem unlikely. Perhaps a future extension of this mammoth analysis will show this trend to be part of a stepwise cooling similar to that which is emerging from studies of the Arctic.

The second line of research nowadays—that of investigating the chains of cause and effect which make up global patterns of climate—is no less impressive in scope.

Sawyer of the Meteorological Office, Bracknell, has already observed that as friction and viscosity are capable of dissipating the total kinetic energy of the atmosphere in about 5 days, the cause of persistent circulation anomalies is unlikely to lie in the dynamic inertia of the circulation (*Tech. Note Wld Met. Org.*, No. 66, 227; 1965). In keeping with his conclusion that anomalies in the temperature of the sea surface are the most important single influence on weather in the long term, much work on persistent circulation anomalies is now centred on the feedback effects of ocean and atmosphere. The elucidation of these effects has been overwhelmingly the result of the work of Namias and Bjerknes in the United States, and the current NORPAX Pacific experiment represents, to a large extent, the culmination of their efforts.

R. R. D.

Insect Virus Transmission

ANIMAL virologists have long been envious of insect virologists for their ability to produce milligram amounts of purified virus with the aid of only a centrifuge and a few caterpillars. Envy is rapidly replaced by a feeling of relief, however, when the animal virologist learns of the technical problems encountered in handling insect tissue culture. Many virologists are, therefore, unaware of the uses to which insect virologists have put their knowledge, particularly in the field of insect pest control.

Apart from relative ease of propagation, insect viruses have a number of properties which make them particularly suitable for use as insecticides. Many of them are rapidly lethal to their hosts, but can be sufficiently specific in host range to leave parasites and predators unaffected. Those which cause the formation of inclusion bodies within infected cells are particularly easy to purify because these bodies, which contain infectious virus particles, are resistant to putrefaction. Thus infected hosts can be resuspended in water, allowed to disintegrate and pure preparations of inclusion bodies can be obtained by the simple procedure of differential centrifugation. These inclusion bodies are large enough to be counted in an ordinary bacterial counting chamber. Dried inclusions are very stable and infectivity persists for long periods in such preparations stored at room temperature. The viruses can, of course, multiply in their hosts and spread to insects unaffected by the initial application. These and other favourable properties have, not surprisingly, stimulated much interest, and field trials, with promising results, have been reported. Before large scale use of these viruses in the field becomes commonplace, however, several problems remain to be overcome, and the article by Longworth, Robertson, Tinsley, Rowlands and Brown on page 314 of this issue of *Nature* illustrates one of these—uncertainty concerning host range within and outside the class Insecta—in a particularly interesting way.

Dramatic control of larval populations of the moth *Gonometa podocarpi* (Lepidoptera: Lasiocampidae) in Uganda has been obtained using a virus which grows in the cytoplasm of larval gut and fat body cells (without forming inclusion bodies). The morphological, biophysical and biochemical properties of this virus closely resemble those of vertebrate picornaviruses and this caused Longworth *et al.* to examine the relationships of the *Gono-*

meta virus to selected animal picornaviruses by immunological techniques. Not surprisingly, no serological relationship between the insect and animal viruses could be demonstrated, but, unexpectedly, precipitating activity in gel diffusion tests with *Gonometa* virus was found to be present in the sera of all pigs examined. Studies on the nature of this activity showed that it was sensitive to 2-mercaptoethanol and that it sedimented in the 19S region of sucrose density gradients. Electrophoresis in agarose and electron microscopy confirmed that the precipitating activity was in fact IgM antibody. No activity was found in the IgG fraction of any serum. Subsequent testing showed antibody against *Gonometa* virus to be present in sera from cattle, sheep, horses, dogs and three species of deer, although no reactions were obtained with sera from guinea-pigs and rabbits reared for laboratory use, with wild rabbits, or with gnotobiotic pigs and cattle.

Longworth *et al.* suggest that the presence of this antibody in British animals may follow their repeated exposure to small amounts of antigen—rather than virus multiplication, explaining the lack of IgG antibody—but point out that at present *Gonometa* virus is only known to occur in an insect indigenous to East Africa and unknown elsewhere. They also point out, however, that only a small number of insects have been examined virologically and suggest that their observations indicate the existence of a virus closely related antigenically to *Gonometa* virus in a host, possibly an arthropod, in the United Kingdom and which regularly reaches mammalian hosts. The authors conclude that the apparent regular transmission of such viruses to mammalian hosts highlights the potential risks arising from the deliberate release of viruses to control insects should the viruses show a wider host range than expected.

None of the viruses studied by insect pathologists has as yet been found to multiply in a non-insect host, though it should be remembered that arboviruses, traditionally studied by animal virologists and classified as animal viruses, multiply—by definition—in both their vertebrate hosts and in their arthropod vectors, and that many viruses pathogenic for plants also multiply in their arthropod vectors. The observations of Longworth *et al.* thus serve to stress the necessity, already apparent on general grounds, of thorough testing of any potential viral insecticide for safety to humans, livestock, wild life and crops.

T. H. P.

Transport of Excitons?

WHEN light in the visible or ultraviolet part of the spectrum is absorbed in a solid, the photon is converted into an excitation of the atoms. It is a very important feature of some electronic excitations that they can be transferred very efficiently from atom to atom and that energy can thus be transported away from an illuminated surface. Such processes are important in fields as diverse as power generation, photography and biosynthesis. Although these concepts of energy transfer can be elaborated theoretically, it is not at all easy to detect this transfer and identify the mode precisely. In the absorption spectrum of a semiconductor or dielectric, one of the most intense absorptions is at an energy slightly less than that of the forbidden energy gap. The theory is that a

photon at this energy is converted into an excited pair consisting of an electron and a hole. The electron and the hole do not drift apart but stay bound to each other. They are not, however, too tightly bound to the parent atom. They represent packets of energy which can, in theory, drift through the network of atoms by means of a very efficient quantum mechanical transfer or "resonant transfer" of energy (Dexter and Knox, *Excitons*, Wiley; 1969). The importance of the exciton configuration is the high level of stored energy (say 6 eV for an alkali halide) and the theoretically long time before recombination.

Although the lifetime of an exciton is expected to be long in an ideal solid lattice, it may be limited to a few nanoseconds in a typical real solid by surfaces and lattice defects; a typical diffusion range is much less than a millimetre. It is, however, difficult to find where an exciton started its life and where it was annihilated. No current flows and no track is left. One is obliged to try to observe the effects of the energy released at annihilation and to eliminate the possibility of other forms of energy transport from the region where the light was absorbed. Several attempts have been made to measure the exciton diffusion length in cadmium sulphide. For example, Broser and Balkanski (*Z. Elektrochem.*, **61**, 715; 1957) illuminated a crystal with a fine spot of light and found that this could produce an electric current between two electrodes in a different region. The migration of energy could, however, possibly be accounted for by absorption and re-emission of light. Another important energy transfer process involving excitons was proposed in a satisfying new model for the formation of F-centres in alkali halides (Pooley, *Proc. Phys. Soc.*, **87**, 245, 257; 1966; Hersh, *Phys. Rev.*, **148**, 928; 1966). In this model, kinetic energy from an exciton annihilation is used to start a focused collision sequence in a crystal which ends with the expulsion of a halogen atom into an interstitial site. Townsend (*Phys. Lett.*, **28A**, 587; 1969) elegantly confirmed that ion motion is indeed involved when he showed that illuminating a very clean crystal of potassium iodide with light in the first-exciton band could produce efficient sputtering. An elaboration of these experiments has now unexpectedly produced an observa-

tion which could be interpreted as exciton motion; the method has more elegance and is probably less ambiguous than earlier experiments.

Al-Jammal, Pooley and Townsend (*J. Phys. C.*, **6**, 247; 1973) recently found that an electron beam of energy of several hundred electron volts gave a surprisingly high sputtering yield in potassium iodide, with an unexpected maximum in the curve of efficiency against energy occurring at 400 eV. This result implies that energy is being transported efficiently to the surface through 25 nm of crystal (the stopping range for 400 eV electrons). Most probably the transport is excitonic. The efficiency is so high that fluorescence and reabsorption are unlikely. Focused collision sequences are again known to be much too inefficient; for example, if 5 eV of kinetic energy is imparted to one atom, at least 1 eV is lost in transferring that energy to the next atom and so on down a chain of atoms. Five stages of transfer would be completed within only 5 nm. Alternatively, interstitial atom diffusion is possible but the effects of thallium ion doping are stronger than would be expected according to this explanation. Thus one is left with exciton diffusion as the most likely mechanism.

Using some approximations to esti-

mate the profile of electron energy deposition, Al-Jammal *et al.* estimate the exciton diffusion length to be about 20 nm. Probabilities of resonant transfer in KI are such that an exciton should jump once every 10^{-12} s on average. For three-dimensional diffusion, the estimated typical range, 20 nm, will be achieved if the exciton lifetime is 2×10^{-8} s. This is of the same order of magnitude as the lifetime estimated by Collins (*J. Appl. Phys.*, **30**, 1135; 1959) and Bleil and Broser (*J. Phys. Chem. Solids*, **25**, 11; 1964) for excitons in cadmium sulphide. Thus a fairly consistent picture emerges. It has been shown that defects serve as traps and recombination centres for excitons in many materials. Thallium in potassium iodide acts in this way and was used in this experiment to check the consistency of the exciton diffusion model. Measurements on a crystal doped with thallium showed a reduced diffusion length of only 13 nm. This result gives a trapping cross-section for the thallium ion which fits well with its ionic radius.

The novelty of the approach derives from the use of a surface phenomenon, namely sputtering, to measure energy release in the lattice, rather than fluorescence, which was used in most of the previous experiments.

A.G.H.S.

Transfer RNAs and Tumour Viruses

RNA tumour virus particles, in addition to containing 60–70S RNA which is presumably the viral genome, contain 4S RNA molecules that have been shown to be transfer RNAs specified by the host cell in which the virus particles matured. Furthermore, it is known that the relative amounts of various species of tRNAs in the virus particles and in the host cells differ, which suggests that the tRNAs in the virions are not simply a representative sample of the tRNAs in the host cell. It is not known why RNA tumour virus particles carry tRNAs, or how they get into the virions during maturation, but in *Nature New Biology* next Wednesday (April 4) Wang *et al.* describe some experiments which indicate that the viral genome may somehow control which species of tRNAs are incorporated.

Wang *et al.* compared the tRNA populations in non-defective avian sarcoma virus particles, SR.RSV, in avian leucosis virus particles, RAV.1, and in Bryan high titre Rous sarcoma virus particles grown in the presence of

RAV.1, which acts as a helper for the replication of the defective Bryan virus to yield phenotypically mixed BH.RSV (RAV.1) particles. They found that the relative amounts and number of species of tRNAs in RAV.1 and BH.RSV (RAV.1) particles differ and that the tRNAs in SR.RSV particles resemble those in BH.RSV (RAV.1) particles. The RAV.1 particles contain not only absolutely more chargeable tRNA molecules than either sarcoma virus but also more species of tRNAs. The pattern of tRNAs in transformed and untransformed chick cells was, however, very similar.

It seems, therefore, that leucosis viruses and sarcoma viruses propagated in the same cells pick up different populations of tRNAs and therefore that the viral genome may exert some control over this incorporation. What part if any the tRNAs play in the life cycle of the viruses still remains to be elucidated, but these experiments do suggest the incorporation of tRNAs is more than a chance event.

CHROMOSOMES

Model of *X* Inactivation

from a Correspondent

THE most interesting explanation yet proposed for the mechanism of *X* chromosome inactivation in mammals has been put forward by Brown and Chandra (*Proc. US Nat. Acad. Sci.*, **70**, 195; 1973). The chief problem in considering *X* chromosome inactivation is to envisage a mechanism which will lead one whole chromosome of an apparently similar pair to become inactive in somatic cells, while the other retains its normal genetic responsiveness. A step forward came with the discovery that in certain marsupials the inactive *X* is always of paternal origin (Sharman, *Nature*, **230**, 231; 1971; Cooper *et al.*, *Nature New Biology*, **230**, 154; 1971). This led Cooper (*Nature*, **230**, 292; 1971) to postulate that the random inactivation of maternal or paternal *X* chromosomes in eutherian mammals has evolved from an earlier simpler system of paternal *X* inactivation.

Although it is still far from clear whether inactivation of paternal *X* is in fact the general rule in marsupials, Cooper's idea is attractive because the sex chromosomes, and indeed the chromatin generally, do seem to become inactive during spermatogenesis; thus, if the paternal *X* remains inactive in the new zygote, this would seem a simpler system than if it were reactivated, and this followed by a random inactivation. In detail, however, Cooper's model contained difficulties and grounds for criticism (Lyon, *Biol. Rev.*, **47**, 1; 1971).

Brown and Chandra's model incorporates the idea of evolution from an ancestral inactivation of paternal *X*, but eliminates many of the difficulties. Basically, they propose a system of two genes controlling the activity of the *X* chromosome; one, sensitive to parental origin, acts on the second, the receptor, which determines the activity of the *X* chromosome. In marsupials, they suggest, both these genes are located on the *X*, so that if an *X* passes through a male gamete its sensitive gene is inactive, and its receptor gene is never activated. During evolution, they next suggest, the transfer of the sensitive gene to an autosome led to *X* inactivation at random in eutherians. Eutherians thus have an autosomal pair of sensitive genes, of which only the one of maternal origin is active. This gene produces "a single informational entity that attaches to a receptor site on one of the *X* chromosomes encountered at random". In other words, the number of active *X* chromosomes in a eutherian is equal to the number of maternally-derived autosomal sensitive genes.

Such a model fits well with many known facts concerning *X* inactivation. In individuals with chromosome anomalies,

if the number of autosomes remains normal, then no more than one *X* chromosome should remain active no matter how many are present and what their parental origin. This is indeed what is observed, even in 2A:XXXXY or 2A:XXXXX individuals. Conversely, if the number of autosomes is disturbed, as in triploids or tetraploids, then the number of active *X* chromosomes should depend on the number of maternal sets of autosomes. In particular triploids could have either two maternal and one paternal set, or one maternal and two paternal, and so should be of two types, with two or one active *X* chromosome(s). This again is observed. Tetraploids, if formed by doubling of chromosomes of an originally diploid zygote, should have two active *X* chromosomes, as indeed they do. The piece of evidence which is least well explained by the model is the preferential non-random inactivities of human *X* chromosomes with deletions. But because the non-randomness in this case could be the result of cell selection rather than disturbance of the inactivation mechanisms, this point is not important.

Thus Brown and Chandra's hypothesis has elegance, simplicity and is in principle eminently testable. Individuals with anomalies of the relevant autosome should have alterations of *X* chromosome activity and the type of alteration will depend on the parental origin of the anomalous chromosomes.

If the model proves to be correct, it will be the first clear instance in mammals of the activity of single alleles in autosomes, except for the immunoglobulins which could be a special case. Nucleolar-organizing regions are sometimes found on only one of an autosomal pair. This might fit with Comings's suggestion (*Amer. J. Hum. Genet.*, **20**, 440; 1968) that active and inactive *X* chromosomes are distinguished by their site of attachment in the nucleus, if a nucleolus rather than the nuclear membrane is the critical site of attachment (Lyon, *Nature New Biology*, **232**, 229; 1971). The active *X* chromosome would be attached to the same nucleolus as the maternal autosome.

One virtue of Comings's model is that it eliminates the need for the unidentified "information entity" which Brown and Chandra postulate, and which does pose something of a difficulty because it must be some unit substance, which can activate only one receptor site. Another general difficulty, met by all models of *X* inactivation proposed so far, is that of explaining how one complete chromosome is activated or inactivated, rather than just a short region. Brown and Chandra's model offers nothing new on this point, hence it has the further endearing quality that, if it should be proved right, there will still be intriguing problems left to tackle.

MYOSIN

Amputating Heads

from our Molecular Biology Correspondent

THE myosin molecule gives the impression of a protein designed by an international committee of protein chemists. It is a chimaera of globular and fibrous parts, contains chains of very high and of low molecular weight, and has complex enzymatic and ligand-binding properties. The long two-stranded α -helical shaft forms part of the lattice of the thick filaments of the myofibril, and the globular heads project out of the filament axis. During the contractile process, when these heads interact with the actin of the thin filaments, their angular orientation changes, but it is by no means clear how this very sizable change in geometry is accomplished. The vague notion of a hinge at some point in the shaft has often enough been invoked, but the evidence in favour of such a region in a superwound double α -helix, behaving hydrodynamically as a rigid rod, has been at best exiguous. There remains, however, the high specificity of tryptic cleavage of the shaft, which occurs about one-third of the way from the end that bears the two globular heads. This has always suggested to the more febrile minds in the field a rather loosely organized segment, or dislocation, in this region. Burke, Himmelfarb and Harrington (*Biochemistry*, **12**, 701; 1973) have now given more tangible expression to such a view.

They have examined the properties of the entire myosin shaft, which can be prepared by shearing off the heads with papain. The time course of hydrolysis of these rods with trypsin can be fitted by three rate processes differing over nearly two orders of magnitude in their apparent velocity constants. The fastest process is presumed to be associated with hydrolysis in a uniquely labile region. Next, thermal melting profiles, in which the diminution of α -helical structure with increasing temperature is followed by means of optical rotation, show clear evidence of biphasicity, with one transition below and another above about 50°C. After digestion through the rapid hydrolysis phase and part of the slower phase, the resulting light meromyosin, comprising the terminal two-thirds or so of the shaft, shows only a single co-operative melting transition. Moreover, below this sharp transition the viscosity of the light meromyosin is invariant with temperature, whereas that of the intact rod falls markedly with increasing temperature even before the first optical transition.

The authors infer from all this that there is in the myosin rod a sizable region of α -helix, which melts more readily than the rest, is relatively flexible and in consequence readily attacked by

proteases. Such a weakly structured region, they hazard, might respond to an applied tension by uncoiling. This extended form will resist any further tension, and might be expected to annihilate it by a condensation process. Burke *et al.* interpret in these terms the biphasic change of tension in a muscle subjected to a rapid change in length, which was recently described by Huxley and Simmons. They have attempted to induce a change in the tendency of the rod to distort by addition of contraction-linked ligands, such as ATP, ADP, and calcium and magnesium ions, though without success.

The indications are that the other α -helical muscle proteins, in particular the molluscan paramyosins, which have no globular heads, are very similar in most important structural respects to the myosin rod, and Halsey and Harrington (*ibid.*, 693) have undertaken a parallel study on clam paramyosin. As with myosin rods, tryptic hydrolysis displays a very rapid initial phase in which a labile region is destroyed. A "light meromyosin" is generated, which melts thermally in a single transition, corresponding to the higher of two transitions observed in the melting of the intact paramyosin. The amino-acid compositions of the two parts of the molecule differ and that of the surviving rod has a higher computed α -helix-forming potential (at least by criteria drawn from analysis of globular protein conformations); indeed the composition of the material released in the early stages of trypsin hydrolysis should in these terms be distinctly unfavourable for the stability of α -helices. This lends support to the possibility of a region of distorted, or at least weakened, α -helix in this molecule. Cowgill in a report last year also showed evidence of two regions in the molecule differing in stability, the stable "light meromyosin" being the N-terminal end.

As to the question of whether and why two heads are in fact better than one, Margossian and Lowey (*J. Mol. Biol.*, **74**, 301; 1973) have set out in search of an answer by preparing, by papain treatment under highly selective conditions, followed by ion-exchange chromatography, one-headed myosin, as well as one-headed heavy meromyosin. Properties such as molecular weights and α -helix contents coincide nicely with the expected values, and the fragments contain their complements of light chains. The mutilated molecules look exactly as they should in the electron microscope. In the accompanying article (*ibid.*, 313), which has all the attributes of a definitive utterance, Margossian and Lowey compare the functional properties of the one and two-headed species as well as isolated heads with no shaft (subfragment-1). The ATPase turnover of the two-headed

protein is, as nearly as it is possible to estimate, twice that of the one-headed derivatives, which indicates the self sufficiency, and to a first approximation independence, of the two heads. The actin-binding stoichiometry, measured with the ultracentrifuge, is one actin subunit per head, in agreement with recent work of Eisenberg and co-workers, and in contradiction of earlier results of Young. A somewhat tortured analysis of the behaviour of unfractionated mixtures of partially inactivated myosins by Toikawa and Morales not long ago led them to the conclusion that both heads of myosin must be operative for superprecipitation with actin. Margossian and Lowey have been able to consign this notion to limbo by showing that their one-headed myosin when mixed with F actin superprecipitates very nicely. Only the time lag is longer, and this may be put down to the greater affinity with which the two-headed species would be expected to interact with the F actin.

The problem of why myosin need have two heads is still unanswered, leaving only some enigmatic fragments of evidence against their precise equivalence. Anybody with a serious interest in the field will want to study the analysis

given by Margossian and Lowey of ATPase activity in relation to actin binding, which goes some way towards clarifying a situation obfuscated by stratum upon stratum of hypothesis.

CONSERVATION

Galapagos Endemics

from our Plant Ecology Correspondent

IN 1971 Wiggins and Porter published a new *Flora of the Galapagos Islands* (Stanford University Press, California) which has provided the raw material and the necessary incentive for the initiation of more extensive research into the flora of these islands. Johnson and Raven (*Science*, **179**, 893; 1973) have subjected the data from this *Flora* to rigorous statistical and phytogeographical analysis.

Only 26 per cent of the Galapagos flora is endemic, a figure which compares poorly with the Hawaiian Islands where more than 90 per cent of the vascular plant species are endemic. The percentage of endemics in the individual floras of the Galapagos Islands is inversely related to the area of the islands, a situation which can be explained by reference to the pattern of

A Persistent Cell Population in the Thymus

THE thymus in the centuries following its first description was regarded as a mysterious organ. Many and bizarre were the functions ascribed to it until the works of Miller and of Good showed that it regulated the development of immunological responsiveness—at least in some species of mammals. Since then it has been revealed that the thymus performs this function by liberation of what have come to be known as T lymphocytes. Much emphasis has been placed by cellular immunologists on this versatile species of cell and its more productive ally (as far as antibodies are concerned), the B lymphocyte. But, aside from its capacity for producing cells, the thymus itself has retained much of its mystery. It is suspected to emit a hormone, but hardly anything is known of the process of differentiation whereby the organ gives rise to T cells. In next Wednesday's *Nature New Biology* (April 4) Elliott deals with heterogeneity of cells within the thymus.

It is usually accepted that after treatment of a mouse with corticosteroids, such as hydrocortisone, there remains in the thymus, after much cell death, a population of steroid-resistant cells. In an earlier report, Elliott *et al.* (*Nature New Biology*, **234**, 77; 1971) showed that these cells were not T cells that had come in from outside the organ but were cells that were in the thymus

at the time of treatment with corticosteroid.

The method involved the engraftment of a chromosomally-marked but otherwise syngeneic thymus graft into a normal mouse and then, after treatment with hydrocortisone, display of the phytohaemagglutinin (PHA)-responsive cells from the graft *in vitro*. Elliott now extends this observation and shows that with or without treatment with hydrocortisone most of the cells in a thymus graft at any time after its emplacement, that can be induced to respond to PHA, are cells that are native to the graft.

The thymus is usually thought of as a staging house through which pass stem cells and their mitotically amplified products. In a thymus graft active mitosis of the native cells in the graft itself ceases by about the twentieth day after grafting and yet, as Elliott shows, many weeks later the PHA-responsive cell population revealed *in vitro* contains many of the native cells which previously would have been assumed to have emigrated to the periphery.

The functional significance of this persistent cell population is not known nor is the morphology of the persistent cell. Immunologists who think of thymocytes as equivalent to peripheral T cells should, however, remember that they are also handling a cell population which never seems to leave the thymus.

vegetation types in the islands. There are three basic zones of vegetation. The littoral zone has a high rate of plant immigration, but also a high rate of extinction. Here there are few endemic species. Lowland areas, which are particularly extensive in the Galapagos and are arid, are rich in endemics. Elevated areas have a moister climate and a low proportion of endemic species. Because the larger islands are also those which possess the regions of greatest altitude, it is to be expected that island areas will be negatively correlated with the proportion of endemics in the flora.

The reason for the frequency of endemics in the arid zone and their scarcity in the moist uplands is probably to be found in the climatic history of the Galapagos Islands. Colinvaux has found (*Nature*, **240**, 17; 1972) that the wet climate of the uplands dates back only 10,000 years. Arid climates, however, have existed on the Galapagos for at least 34,000 years and probably for much longer than this. Long established taxa are therefore liable to be adapted to arid conditions.

Some species of the moist, elevated areas, however, are endemic, for example, the tree *Scalesia pedunculata* and the shrub *Miconia robinsoniana*. Concern about the future of plants such as these on the Galapagos is expressed by E. K. Schofield (*Biol. Conserv.*, **5**, 48; 1973). Because the uplands receive most of the available rainfall, it is these areas which are subjected to the most intensive cultivation by the 3,000 human occupants of the islands. Not only does this involve the physical clearance of natural vegetation, but it has also resulted in the spread of exotic species introduced by man. Many of these exotics, such as *Phlox* and *Ricinus*, seem to be spreading from the disturbed areas into the natural plant communities. It is widely recognized that island faunas are particularly sensitive to the introduction of non-native species and undoubtedly the same is true of plants, though this is less well documented. It is to be hoped that an adequate conservation policy will be introduced into the Galapagos before irreparable harm ensues and the extinction of endemic plant species results.

PESTICIDES

Atmospheric Distribution

from a Correspondent

THE factors which affect the distribution of pesticides throughout the atmosphere were discussed by members of the Physicochemical and Biophysical Panel and the Pesticides Group of the Society of Chemical Industry at a symposium held on March 6 at the society's rooms in London.

Dr R. A. E. Galley (Chairman of the

Pesticides Group) reviewed the factors which cause pesticides to enter the atmosphere. Vaporization can occur from falling spray particles and from plant, water and soil surfaces. Transport by winds can occur over very large distances and the vapours can be deposited onto the Earth's surface in rain water. Although the concentrations of organochlorine particles in air or rain water are usually between 1 and 20 parts in 10^{12} the first mile of the atmosphere could contain up to 8,000 tons of these pesticides.

Dr C. A. Edwards (Rothamsted Experimental Station, Harpenden) considered that the high rates of loss of pesticides from soils often observed soon after application might be explained by volatilization. He said that this process had received relatively little consideration in the past but there are signs that it is beginning to receive more attention now. Dr F. T. Philips (Rothamsted Experimental Station, Harpenden) described his work on the volatilization of pesticides from glass and plant surfaces, from which it was clear that the interaction of adsorption, wind speed, crystal size and temperature is very complex.

Dr D. A. M. Watkins (Long Ashton Research Station, Bristol) discussed the implication of the vapour phase photochemical decomposition of pesticides. It is known that many pesticides are decomposed by short wavelength radiation and it was pointed out that although the spectrum of radiant energy which reaches the Earth's surface is very narrow, photochemical reactions could play an important part in degrading pesticides which had diffused to the upper atmosphere.

The global transport of pesticides by birds was the theme of the talk by Dr P. R. Evans (University of Durham). A recent estimate suggests that 5,000 million song birds migrate from Europe and Siberia to Africa south of the Sahara each year. About 1,500 million die in Africa, thereby depositing pesticide residues which originated in northern latitudes. Calculations show that 7–11 kg of DDT is transported in this way each year.

Professor R. S. Scorer (Imperial College, London) suggested that the current philosophy of spraying crops to protect them from insect pests is highly inefficient and analogous to spraying human beings to protect them from malaria. He said that pests must be controlled on a regional international basis and that this would enable meteorologically-induced macro swarms to be tracked down and attacked. Much more biological knowledge of the life cycle of insects is required and this has to be related to a whole range of scientific disciplines. This contribution aroused a great deal of controversy but its concepts were well supported by radar photographs which showed that very many species of insect do in fact occur in large numbers in the atmosphere.

Further support for Professor Scorer's suggestion came from Dr R. C. Rainey (Centre for Overseas Pest Research) who described the way in which meteorological conditions have been used to enhance the distribution of pesticides when applied by ultra low volume techniques. He quoted the highly efficient controls of desert locust and African army worm that have been obtained by the use of dieldrin.

Induced Replication of Satellite DNA

WHEN mouse cells in culture replicate their DNA prior to mitosis, the satellite DNA fraction of the cell genome, which is defined by its comparatively simple base sequence, is replicated late in the S phase of the cell cycle after the bulk of the non-repetitive DNA has replicated. It is not surprising therefore that considerable interest was aroused in 1970 by Smith, who reported that when baby mouse kidney cells are infected by polyoma virus, satellite DNA replicates early in the S phase before the remainder of the DNA.

This observation by Smith seemed to indicate that polyoma virus somehow alters the sequence in which different fractions of the cell genome are replicated, an observation with many implications for models of DNA replication in mammalian cells. Unfortunately, however, as Hatfield and Walker report in *Nature New Biology* next Wednesday

(April 4), Smith's results are not "readily reproducible".

Hatfield and Walker, as a preliminary to further investigating this phenomenon, decided to repeat Smith's experiments keeping conditions as close as possible to those he used. They obtained polyoma virus from Smith, for example, and then used it to infect confluent cultures of non-dividing baby mouse kidney cells. Infection resulted in a stimulation of cell DNA synthesis, but in eleven experiments Hatfield and Walker failed to detect preferential early replication of light satellite DNA.

There seems to be no satisfactory way of reconciling Smith's results with those of Hatfield and Walker, and the latter group is forced to the conclusion that the time of replication of satellite DNA in these mouse cells, stimulated to divide by being infected by polyoma virus or by being exposed to serum, is similar.

TUMOUR VIRUSES

Viral Proteins

from our Cell Biology Correspondent

WHEN simian virus (SV) 40 infects and transforms non-permissive cells—cells which do not support replication of the viral genome—the SV40 DNA becomes integrated into the DNA of a host chromosome(s). Usually the whole viral genome must be integrated because SV40 can be rescued from cells of most clones of transformants by fusing them with permissive monkey cells. Furthermore, the integrated viral genome is transcribed in the transformed cell, even though it is not replicated independently of host chromosomes, because viral RNA can be detected in the nucleus and cytoplasm. Presumably these viral RNA transcripts act as messengers for those proteins which cause transformation.

Obviously tumour virologists would dearly like to isolate the transformation-inducing viral proteins; that hard task remains to be done, but considerable progress has been made towards analysing the pattern of transcription of the integrated viral genome. This is technically easier to do, of course, because the two strands of the viral DNA can be separated and specifically fragmented to yield probes specific for viral RNA sequences. Khoury and Martin and their colleagues at the National Institutes of Health (Khoury *et al.*, *J. Virol.*, **11**, 54; 1973), for example, have reported an analysis of the SV40 RNA made in eleven clones of SV40 transformed cells of various species (mouse, human, sheep, rat and hamster). In nine of these eleven clones the cells contain RNA transcribed from 37 to 50 per cent of the strand of SV40 DNA that is transcribed at early times during the replication of the virus in permissive monkey cells. In two other clones the cells contained transcripts corresponding to 65–75 per cent of this early or minus strand of the SV40 DNA. It seems therefore that in transformed cells all the SV40 early genes are transcribed, together with variable amounts of the early strand DNA not transcribed in permissive cells. In nine of the eleven clones the cells contained no detectable amounts of RNA transcribed from the complementary late or plus strand of the viral DNA which is transcribed after the commencement of DNA replication during the lytic cycle. It may well be therefore that in these transformed cells late genes are not transcribed at all but the possibility that the late genes are transcribed and then the transcripts are rapidly degraded has not been ruled out. In two other clones the cells contain some late RNA but it corresponds to less than 8 per cent of the late strand DNA.

These data, and similar data that have

been obtained by Keller and Sambrook and were reported at the recent Lepetit meeting, rule out the possibility that the late genes of SV40 are involved in specifying transformation proteins. Either, therefore, the early genes that are also expressed during the lytic cycle specify transformation proteins or possibly anti-late RNA transcribed from segments of the early or minus strand of DNA that are not transcribed during the lytic cycle specify transforming proteins.

Because there is no clue as to the nature of the transforming gene protein(s) and because cells infected by SV40 and its close relative polyoma virus continue to make their own proteins, it is wellnigh impossible to fish out viral proteins other than capsids from infected cells. Several groups have therefore tried to identify viral proteins made in cell free systems that support coupled transcription and translation of viral DNA. Crawford and Gesteland (*J. Mol. Biol.*, **74**; 627; 1973), for instance, have programmed a coupled *Escherichia coli* cell free system with polyoma virus DNA and have detected the synthesis of polypeptides of various sizes including a polypeptide that corresponds in size to the major protein of the virion. Fingerprint analyses of tryptic digests of this *in vitro* polypep-

tide indicate that it is indeed related to the major protein of the capsid, and many of the smaller polypeptides made *in vitro* probably correspond to incomplete capsid protein molecules. But all of the polypeptides made *in vitro* also contain amino-acid sequences not present in the major capsid protein made *in vivo*. Crawford and Gesteland conclude therefore that "The aim of characterizing all the polypeptides coded for by polyoma virus DNA and synthesized *in vitro* will almost certainly require the development of a more homologous system". They might also have added that even when systems which support coupled transcription and translation of polyoma DNAs are obtained from mammalian cells the task of identifying anything other than the major capsid protein will remain formidable.

The juxtaposition in the *Journal of Molecular Biology* of Crawford and Gesteland's article with that of Varmus *et al.* (*ibid.*, 613) serves to underline the comparative ease with which tumour virus nucleic acids can these days be detected in host cells and the difficulty in detecting tumour virus proteins. Varmus *et al.* set out to detect the DNA proviruses of Rous sarcoma virus in four lines of mammalian cells trans-

Messenger Specific Initiation Factors in Eukaryotes

STUDIES on the translation of mammalian mRNAs in heterologous cell-free systems and *in vivo* in amphibian oocytes have suggested that the initiation factors required for translation of eukaryotic mRNAs are common to a large number of cell types. Globin mRNA, however, can only be translated on embryonic chick muscle ribosomes in the presence of reticulocyte initiation factor IFM₃ which binds mRNA to ribosomes. Does tissue specificity exist at the translational level? This is the question tackled by Wigle and Smith in next Wednesday's *Nature New Biology* (April 4).

Wigle and Smith used a fractionated cell-free system from Krebs II ascites cells to study the translation of a number of natural mRNAs. They isolated and purified from a ribosome-free ascites supernatant a cytoplasmic initiation factor (IF_{EMC}) required for the translation of encephalomyocarditis viral RNA (EMC RNA). Use of sparsomycin, which inhibits chain elongation, and examination of the initiation peptides by high voltage electrophoresis, showed that IF_{EMC} is required for initiation on EMC RNA and that such initiation occurs at the correct initiation site.

IF_{EMC} factor is specific for EMC RNA translation and is not required for translation of synthetic polynucleotides. Translation of globin mRNA in the fractionated ascites cell-free system is only slightly stimulated by addition of

factor. Addition of another ascites cytoplasmic fraction EF-1, however, did stimulate globin synthesis, suggesting the presence of a globin initiation factor(s) in this fraction. Translation of bacteriophage MS-2 RNA in the ascites system is not stimulated by purified IF_{EMC} but stimulation does occur in the presence of crude supernatant. Thus a factor(s) exists in the crude ascites supernatant which can direct the initiation and translation of MS-2 RNA.

Several other workers have detected initiation factors in the cytoplasm of eukaryotic cells but these seem to be involved in the binding of initiator tRNA to ribosomes. The results of Wigle and Smith indicate the presence in ascites cytoplasm of messenger-specific factors required for the recognition of specific natural mRNAs. If the number and relative amount of each factor vary in different tissues, this could account for the observed tissue specificity in the translation of mRNA. Thus the undifferentiated oocyte may contain many factors for the many classes of mRNA produced in early embryogenesis, whereas a more differentiated cell may have lost factors specific to classes of mRNA no longer required for its function. That the factors may not be absolutely specific is indicated by the success in translation of mRNAs in heterologous systems achieved by other workers.

formed by two strains of Rous sarcoma virus. By measuring the rate of reassociation of mixtures of denatured DNA from the transformed cells and DNA reverse transcribed from Rous sarcoma virus RNA, they have estimated that in both transformed rat and transformed mouse cells there are two genome equivalents of Rous sarcoma virus DNA per cell genome. Furthermore, this viral RNA is associated with cell DNA of high molecular weight which suggests that the proviruses are covalently integrated in cell chromosomes.

LASERS

Identifying Transitions

from a Correspondent

THE assignment of molecular infrared and ultraviolet spectra will be much assisted and the detailed knowledge of molecules much enhanced if a laser spectroscopy technique proposed by Skribanowitz, Kelly and Feld of MIT (*Phys. Rev.*, **6**, 2303; 1972) can be realized experimentally.

In general, infrared spectra result when molecules are raised from their ground state to some vibrationally excited state through the absorption of radiation and each vibrational state of a gaseous molecule has an associated set of closely-spaced rotational energy levels labelled with rotational quantum numbers, J . By virtue of simultaneous changes of rotational state during a vibrational transition, gas phase infrared spectra can exhibit a fine structure. Except for the simpler molecules, this rotational fine structure is rich, complex and often unresolved by conventional spectroscopic techniques, notwithstanding the severe restriction that only those changes of rotational quantum number, J , of -1 , 0 and $+1$ between the lower and upper vibrational states (called P, Q and R branch transitions respectively) are permitted. Even if resolution is possible, the unambiguous assignment of J values to the upper and lower state of a component transition can be a difficult problem. Similar, but often more extreme, difficulties are encountered in attempts to analyse rotational substructure of electronic spectra in the visible and ultraviolet regions.

The group at MIT propose a simple technique to solve the assignment problem while simultaneously taking care of resolution difficulties. The necessary requirements are that two component transitions A and B of the fine structure of, for example, a vibrational band share a common rotational level in the upper state and that A exceeds B in frequency. A high powered, monochromatic laser (called the pump), of such frequency and power both to induce molecules to undergo transition A and to saturate it, acts on a low pressure gas. Molecules

in the gas have a spread of velocities, given by the Maxwell-Boltzmann distribution, relative to the direction of the incident radiation and therefore the wavelength at which they absorb the radiation will be shifted by the Doppler effect to different extents by different molecules, leading to the so-called Doppler broadened absorption profile for the transition. On account of the laser monochromaticity and the sharpness of molecular energy levels in a low pressure gas, however, only molecules within a tiny velocity range can be excited to the common upper state, for all other molecular velocities shift the incident wavelength away from resonance.

If a low powered laser beam, collinear with the pump, is now tuned over the absorption profile of transition B, the selective increase in population of the shared upper level manifests itself as a decrease in absorption (called the change signal) in a narrow region of the Doppler broadened absorption curve of B. The two crucial properties of the change signal are its sharpness and the symmetrical structure it exhibits when (but only when) A exceeds B in frequency. The sharpness ensures high resolution, and the number, spacing and relative intensity of the symmetrical components reveal the J values to be assigned to the levels involved in transitions A and B.

The reasons for the structure of the change signal and its usefulness in spectral assignment are readily understood. In the absence of an external

field a molecular rotational state of quantum number J is really the superposition of $(2J+1)$ substates of identical energy, each labelled by one of the sub-quantum numbers $M=J, J-1, \dots, 0, \dots, -J$. When the pump and probe laser beams are polarized in parallel directions, transitions A and B only occur between states of the same M and therefore the initial three-level system is actually the superposition of several independent three-level subsystems, each characterized by a different value of M . Under the influence of the saturating pump laser, the change signal associated with a given subsystem M splits into a symmetrical doublet whose separation depends only on the magnitude of M , the values of J for transition A and the laser field strength. Thus, each subsystem produces a doublet of different splitting and the total change signal is clearly a set of symmetrical peaks with a common centre.

The MIT group thoroughly discuss the structure of the change signal as an aid to spectral assignment and in particular they show how relative intensities among the subsystem doublets depend both on M and on the three J values involved in the transitions A and B. Distinctively different patterns can occur for the various possible combinations of transition type (P, Q or R branch) for A and B. The number of components in the change signal is, of course, another clue to the values of J , for the doublet splittings are indepen-

Surface Properties of Lymphocytes

THERE is an increasing number of ways of describing lymphoid cells. Two reports in next Wednesday's *Nature New Biology* (April 4) by Rowe *et al.* and by Lippman offer two more such methods.

Surface-bound immunoglobulins have been known to characterize a proportion of normal peripheral blood lymphocytes in both mice and men for some time. Immunoglobulins of all classes have been described and there is evidence for both immunoglobulin class restriction on some cells and lack of such restriction on others. The result obtained tends to depend on the method of demonstration. It is usually supposed that immunoglobulin-bearing lymphocytes are B cells of bone-marrow origin and that their surface globulins are receptors which facilitate the production of antibody by the cells which bear them. Rowe and his colleagues make the observation that a high percentage of lymphocytes (14 per cent) from human cord blood carry IgD on their surface, whereas adult humans have only four per cent of their lymphocytes so coated. The significance of this observation, which has been made in two different centres, is obscure as is the functional significance of IgD itself.

Lippman describes measurements of steroid binding protein (SBP) on various populations of human peripheral blood lymphocytes from normal persons and from those with various kinds of leukaemia. The method is a competitive binding assay using radioactive steroids *in vitro* on a cytosol preparation. It is shown how the SBP levels of lymphocytes from patients with acute lymphoblastic leukaemia (ALL) can be considerably higher than those of lymphocytes from normal volunteers. In patients with ALL, who have been treated with glucocorticoids (among other chemotherapeutic agents), however, the levels of SBP were consistently lower than those of untreated patients.

The object of the study was to obtain a method for the prediction of which patients might respond to treatment with glucocorticoids—those with high SBP levels—and in this respect the work seems highly promising. There is, however, a possible spin-off for the cellular immunologists in that T (thymus-derived) and B cells might differ in their SBP levels and that this difference could relate to differences in their sensitivities to glucocorticoids.

dent of the sign of M and there are at most $(2J+1)$ subsystems of different M if J is the smallest of the values involved. Detailed line shapes for the patterns expected in the experimentally favourable cases of ammonia and hydrogen fluoride are also calculated by Skribanowitz and his colleagues, so that all that remains to be seen is whether such effects will be detected and how useful they will be for molecules of more complex and less well known spectra.

ELEMENTARY PARTICLES

Protons and Partons

from a Correspondent

THE Royal Society had a lot to contend with when it held its meeting on proton scattering at very high energies on March 8. For one thing the windows were vigorously shaken during the afternoon session by the car bomb in Whitehall, about a quarter of a mile away. It was, nevertheless, an absorbing meeting.

Three new devices have greatly extended knowledge of high energy collisions. The Russian 70 GeV/c accelerator at Serpukhov has provided precise data on elastic scattering and extensive bubble chamber data on particle production processes. The 300 to 400 GeV/c machine at the National Accelerator Laboratory (NAL) near Chicago has been running for about a year, and the first-generation experiments at the CERN intersecting storage rings (ISR) near Geneva are nearing completion. These machines take one from a laboratory beam energy of about 30 GeV, at the CERN proton synchrotron and the Brookhaven alternating gradient synchrotron, to the equivalent of about 2,000 GeV at the ISR. As Professor G. Cocconi (CERN) put it in his introductory talk, matter can now be studied at densities more than 100 times greater than the density in the nucleus, although the opportunity does not last for more than about 10^{-24} s. Only in the initial "big-bang" at the formation of a universe, or possibly in the "black hole" at the death of a large star, is such a density thought to be reached for a longer time.

Many of the data which were reported from the new machines cannot yet be explained theoretically, but there has been considerable progress since the international conference at NAL last summer. A potentially exciting suggestion comes from the ratio of positive to negative particles produced with large transverse momenta at the ISR. There is a clear excess of positive particles. The simplest explanation of this is that in the most "head-on" of proton-proton collisions, the constituent particles (or partons) which form the two protons make violent direct collisions with one

another and go off at large angles. In the commoner "peripheral" collisions the individual partons are thought to act collectively. If there are only a few partons (three, for example) in each proton, then the fact that the proton has a positive charge requires a significant excess of positive over negative partons. The parton masses are apparently very large, for they have never been observed directly, but if the underlying process is a collision of mostly positive partons, the ordinary secondary particles observed at large angles will also be more positive than negative. If the number of partons in a proton were large, say thirty, then the fact that a proton has a single unit of positive charge would only have a small effect on the relative number of positive and negative partons, and hence could not be expected to bias the observed charge at large transverse momenta. There is no satisfactory model on which to base exact calculations of the effect, but this proton-proton scattering result fits in well with data on neutrino and anti-neutrino scattering obtained in the Gargamelle bubble chamber at CERN. Both experiments suggest that there is a small number of partons in a proton, and it is therefore possible that the partons may be "quarks" of relatively

simple type suggested by Gell-Mann and Zweig in the early 1960s.

Another result from the ISR has allayed fears that the new machines would only probe deeper into "asymptopia", the energy region in which all measurable parameters would settle down to approach to a limiting behaviour. At Serpukhov energies, all total cross-sections seemed to be tending to a constant, but experiments at the ISR have revealed that the proton-proton cross-section goes up again by 10 per cent (see *Nature*, **242**, 233; 1973). Nobody knows why, although it may be associated with the increased range of masses available for diffraction dissociation as the energy increases. Other surprising results are the behaviour of the real part of the forward scattering amplitude, which seems to be passing through zero at the lower ISR energies but which may become positive at the highest energy, and the large numbers of particles produced with large transverse momenta. Some features of the data do agree well with previous predictions, the "scaling" behaviour of single particle distributions with energy for instance, but all the indications seem to be that a new region of physics is being opened up rather than that a predictable continuation of the old region is occurring.

Wolf-Rayet Systems and X-ray Binaries

MASSIVE X-ray binaries and Wolf-Rayet (WR) systems may represent different stages in the evolution of the same kind of object. In next Monday's *Nature Physical Science* (April 2) van den Heuvel lists the basic parameters of the five X-ray sources known to be associated with binary systems and compares these with parameters of nine double-lined and eclipsing WR binaries with known orbits. He argues that the large mass and intense radiation from the secondaries in the X-ray systems suggest that these are black holes or neutron stars, produced by the evolution of normal massive close binaries.

In such a system, mass is transferred from the primary to the secondary as it evolves, so that the primary becomes an almost pure helium star. The secondary grows to become a hydrogen-rich OB star, and the helium star ends its life as a type II supernova some 1.7×10^6 yr or less after the first stage of mass exchange; the residue, now the secondary of the evolved system, is a black hole or neutron star. Further evolution of the new primary leads to mass transfer on to this object and the production of X-rays 4 to 6×10^6 yr after the supernova event.

This is a commonly painted picture. But van den Heuvel now points out that during part of this evolutionary pattern the system is very like a WR binary. He has calculated the final

binary periods resulting from spherically symmetric explosions of typical WR stars, assuming a remnant mass of either $M_{\odot}$ or $4 M_{\odot}$. The test masses were chosen because the mass of the secondary in Cen X-3 is less than $0.84 M_{\odot}$ and the mass of the secondary in Cyg X-1 is at least $4 M_{\odot}$. For two known WR binaries, V 444 Cygni and CQ Cephei, these calculations indicate final periods close to those of the X-ray binaries. Four other WR systems could, it seems, evolve into X-ray binaries with periods only slightly greater than that of 2U 0900-40 (8.96 day).

The delay between supernova explosion and activity of the X-ray source is sufficient to explain why no supernova remnant is seen associated with the X-ray sources, and it is interesting that if this evolutionary model is correct then there should be X-ray binaries with periods in the range 10 to 150 day. Van den Heuvel points specifically to the source 2U 0525-06, which is relatively weak ($\sim 10^{33}$ erg s $^{-1}$) and has been identified with the spectroscopic binary θ^2 Orionis, which has a period of 21 day and in which the primary is not yet filling its Roche lobe.

The model is certainly attractive qualitatively, but the evolution of massive close binaries which engage in large scale mass transfer is far from being well understood quantitatively.

UNIVERSAL ISOTROPY

Essential Requirement for Life?

by our Cosmology Correspondent

Two fundamental problems each provide common cause for discussion among cosmologists. Why is the Universe isotropic? Is the Universe bound or unbound? Now, Collins and Hawking (University of Cambridge) suggest that the isotropy of the Universe is a direct result of its expansion with a velocity just on the border between infinite expansion with more than the escape velocity and eventual collapse under the gravitational influence of the whole system. Further, they argue that galaxies can only grow in such a universe, and that therefore the presence of life is a direct consequence of the isotropy of the Universe—or at least, the two have a common cause (*Astrophys. J.*, **180**, 317; 1973).

To take the second common question first, the problem of the Universe being bound or unbound is simply one of the velocity of expansion of the Universe in relation to the escape velocity (throughout this discussion a big-bang origin is assumed). The amount of matter in the Universe inferred from observations of bright galaxies is not sufficient to close the system and prevent ultimate expansion to infinity. But there could well be enough dark matter—cool gas, black holes, or even neutrinos—to do the job. Because this dark matter is by definition invisible from Earth, there is plenty of scope for discussion.

Too little is known about the Universe for the discussion to be closed yet. But another topic which has now been closed for discussion is the question of the isotropy of the Universe. With the discovery of the microwave background radiation, and the growing conviction that this is indeed a relic of the big-bang, ever more sophisticated measurements have shown that the radiation, and hence the Universe, is isotropic. One of the most recent measurements, reported by Parijskij, sets as a limit that there are no fluctuations of the blackbody background above the 0.8×10^{-4} K r.m.s. level at 2.8 cm on scales of 3 arc min to 1 arc deg (*Astrophys. J. Lett.*, **180**, L47; 1973). The temperature of the radiation is about 2.7 K, so the accuracy of these measurements is indeed good.

Given that the Universe is isotropic, then, what can be deduced about its origin and other parameters? One difficulty which arises is that if the Universe is homogeneous and isotropic—like the Robertson-Walker model—how do local inhomogeneities such as galaxies and stars grow up? As Collins and Hawking point out, the usual way in which this problem has been tackled is by studying the growth of small perturbations in a Robertson-Walker back-

ground. But perturbations grow disappointingly slowly in a Robertson-Walker universe, and this has led, for example, to suggestions that the original state of our Universe was one of extreme chaos and irregularity. Certainly not all initial conditions would lead to a universe like the one in which we live.

Even worse, initial inhomogeneities should lead to eventual anisotropy. Collins and Hawking have tackled the problem from a different point of view, adopting the philosophy attributed to Dicke and Carter that there is not just one universe but an infinite ensemble of universes, so that all the peculiarities in which mathematicians delight can have a physical being. Only those universes which contain galaxies can have intelligent life, say Collins and Hawking, and galaxies will not occur in highly anisotropic universes.

The philosophy is supported by the mathematics. It turns out that spatially homogeneous model universes can be divided into three classes: those which expand at below the escape velocity and eventually collapse; those which expand

at just about the escape velocity; and those which expand with more than the escape velocity. Those in the first class do not exist long enough to become isotropic, and in any case there is probably insufficient time for galaxies to grow in them during the expansion phase. The third class do not tend towards isotropy, according to Collins and Hawking, and in any case initial perturbations will not grow in density because they too will be expanding more rapidly than the local escape velocity.

That leaves a small class of models, not unlike Robertson-Walker models, expanding at the critical escape velocity and tending towards isotropy. Only in these universes can initial perturbations grow into galaxies. As Collins and Hawking put it, the answer to the question "Why is the Universe isotropic?" is "Because we are here". That seems to be putting the cart before the horse; I would prefer to answer the question "Why are we here?" by saying "Because the Universe is isotropic". But however one splits that particular hair, the point is that we are here, the Universe is isotropic, and that such a situation can indeed be explained with sensible cosmological assumptions.

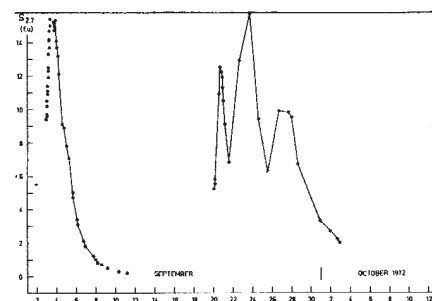
Is Cyg X-3 Similar to Sco X-1?

THE Cyg X-3 radio flare "closely resembles outbursts which are frequently observed to take place in radio galaxies and quasars", write Braes *et al.* in next Monday's *Nature Physical Science* (April 2). The energies involved in this outburst from a small source within our Galaxy are, of course, several orders of magnitude less than those associated with the violent extragalactic events. But Cyg X-3 is only about 10 kpc away from Earth, and its angular size (0.01 arc s on September 24) implies an expansion velocity of 0.2 *c*. Several active extragalactic sources have shown evidence of similarly high expansion velocities, and indeed such sources often consist of at least two components. Braes *et al.* point out that it is possible that an event similar to that observed in Cyg X-3 last year could have produced the triple structure seen in the radio source associated with Sco X-1.

All this speculation arises from an analysis of detailed observations of Cyg X-3 during September and October 1972 at 1.4 and 2.7 GHz, using the Westerbork synthesis telescope and the Effelsberg 100-m instrument. The observations provide further support for the view that Cyg X-3 lies either within or behind the hydrogen emission feature at -68 km s^{-1} (see also Lauqué *et al.*, *Nature Physical Science*, **241**, 94; 1973). Together with kinematic evidence, this means that the distance to the source is at least $10 \pm 1.5 \text{ kpc}$; the radio observa-

tions suggest that Cyg X-3 is not much further away than this.

More details of the multiple structure of the radio flare are also presented by Braes *et al.* The first event, which lasted from September 3 to 10, was a simple outburst consistent with an expanding synchrotron source. The second event was more complex and violent, with three distinct maxima. The first flare (September 3) was similar to the first component of the second event, but the second and third components of that event lasted twice as long and cannot be explained in terms of a repetition of the same process with different energies on the basis of the data available so far. It is not yet possible to say whether the longer durations are a result of smooth injection or repeated discrete injection events. Cyg X-3 now seems to have returned to its normal state.



Observations of Cyg X-3 flares at 2.7 GHz with the Max Planck 100-m telescope at Effelsberg.

Mental Illness as a Metaphor

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This article is a slightly modified and expanded version of Professor Szasz's introductory remarks on the BBC television programme *Controversy*, recorded at the Royal Institution on July 27, 1972, and broadcast on October 2, 1972.

ABOUT twenty years ago I began to clarify what seemed to me the core problem of psychiatry—namely, the nature of so-called mental illness. This led to a systematic scrutiny and refutation of the two fundamental claims of contemporary psychiatrists — that mental illnesses are genuine diseases, and that psychiatry is a *bona fide* medical speciality¹⁻².

It is impossible to undertake an analysis of the concept of mental illness without first coming to grips with the concept of ordinary or bodily illness. What do we mean when we say that a person is ill? We usually mean two quite different things: first, that he believes, or that his physician believes, or that they both believe, that he suffers from an abnormality or malfunctioning of his body; and second, that he wants, or is at least willing to accept, medical help for his suffering. The term "illness" thus refers, first, to an abnormal biological condition whose existence may be claimed, truly or falsely, by patient, physician, or others; and second, to the social role of the patient, which may be assumed or assigned.

If a person does not suffer from an abnormal biological condition, we do not usually consider him to be ill. (We certainly do not consider him to be physically ill.) And if he does not voluntarily assume the role of one who is sick, he is not usually considered to be a medical patient. This is because the practice of modern Western medicine rests on two tacit premises—namely, that the physician's task is to diagnose and treat disorders of the human body, and that he can carry out these services only with the consent of his patient. In other words, physicians are trained to treat bodily ills—not economic, moral, racial, religious, or political "ills". And they themselves (except psychiatrists) expect, and in turn are expected by their patients, to treat bodily diseases, not envy and rage, fear and folly, poverty and stupidity, and all the other miseries that beset man. Strictly speaking, then, disease or illness can affect only the body. Hence, there can be no such thing as mental illness. The term "mental illness" is a metaphor.

Origins

To understand current psychiatric practices, it is necessary to understand how and why the idea of mental illness arose and the way it now functions. In part, the concept of mental illness arose from the fact that it is possible for a person to act and to appear as if he were sick without actually having a bodily disease. How should we react to such a person? Should we treat him as if he were not ill, or as if he were ill?

Until the second half of the nineteenth century, persons who imitated illness—that is, who claimed to be sick without being able to convince their physicians that they suffered from *bona fide* illnesses—were regarded as faking illness

and were called malingerers; and those who imitated medical practitioners—that is, who claimed to heal the sick without being able to convince medical authorities that they were *bona fide* physicians—were regarded as impostors, and were called quacks.

As a result of the influence of Charcot, Janet, and especially Freud, the perspective, both medical and lay, on imitations of illness and healing was radically transformed. Henceforth, persons who imitated illness—for example, who had "spells"—were regarded as genuinely ill, and were called hysterics; and those who imitated physicians—for example, who "hypnotized"—were regarded as genuine healers, and were called psychotherapists. This profound conceptual transformation was both supported and reflected by an equally profound semantic transformation—one in which "spells", for example, became "seizures", and quacks became "psychoanalysts".

A few brief quotations from Freud's early writings must suffice to support my contentions. In 1893, Freud wrote that "hysteria has fairly often been credited with a faculty for simulating the most various organic nervous disorders". While seeming to offer a simple description of the characteristics of the disease called "hysteria", Freud here falsifies the historical record.

Most of the contemporaries and predecessors of the young Freud credited not hysteria but malingerers with the "faculty for simulating. . . ." Indeed, being an abstraction and a name, hysteria cannot simulate or imitate anything; only persons can. Nor is this an isolated figure of speech or stylistic peculiarity of Freud's; on the contrary, it is a part of his systematic strategy for reifying and personalizing pseudomedical labels, and for stigmatizing and depersonalizing persons. Thus, in the very same paper Freud asserts that ". . . hysteria behaves as though anatomy did not exist or as though it had no knowledge of it". But hysteria neither behaves nor knows; only persons do.

In the same year, Breuer and Freud made their now famous announcement that "hysterics suffer mainly from reminiscences"⁶. Here we are offered a metaphorical expression as if it were a literal one: for in the context in which it occurs, the statement implies that hysterics suffer from reminiscences in the same way as arteriosclerotics suffer from hardening of the arteries. But reminiscences are not real lesions; nor, therefore, are hysterics real patients.

Lastly, in a paper published in 1909, Freud acknowledges that the hysteric fakes illness. By then hysteria was well-enough established as a legitimate illness; and Freud did not use such direct language to say so. What he said was that ". . . (hysterical) attacks are nothing else but phantasies translated into the motor sphere, projected on to motility and portrayed in pantomime"⁷. In plain English: hysteria is the dramatic imitation of illness. Nevertheless, Freud would have us believe that hysteria is itself an illness.

The upshot of this psychiatric-psychoanalytic "revolution" is that, today, it is considered shamefully uncivilized and naively unscientific to treat a person who acts or appears sick as if he were not sick. We now "know" and "realize" that such a person is sick; that he is obviously sick; that he is mentally sick.

But this view rests on a serious, albeit simple, error:

it rests on mistaking or confusing what is real with what is imitation; literal meaning with metaphorical meaning; medicine with morals. In other words, I maintain that mental illness is a metaphorical disease: that bodily illness stands in the same relation to mental illness as a defective television set stands to a bad television programme. Of course, the word "sick" is often used metaphorically. We call jokes "sick", economies "sick", sometimes even the whole world "sick"; but only when we call minds "sick" do we systematically mistake and strategically misinterpret metaphor for fact—and send for the doctor to "cure" the "illness". It is as if a television viewer were to send for a television engineer because he dislikes the programme he sees on the screen.

Mental Illness and Psychiatry

Such considerations lead to two diametrically opposed points of view about mental illness and psychiatry. According to the traditional and at present generally accepted view, mental illness is like any other illness; psychiatric treatment is like any other treatment; and psychiatry is like any other medical speciality. According to the view I have endeavoured to develop and clarify, however, there is, and can be, no such thing as mental illness or psychiatric treatment; the interventions now designated as "psychiatric treatment" must be clearly identified as voluntary or involuntary: voluntary interventions are things a person does for himself in an effort to change, whereas involuntary interventions are things done to him in an effort to change him against his will; and psychiatry is not a medical but a moral and political enterprise.

Whereas illness is something a patient has or claims to have or is said to have, treatment is something a physician does or claims to do. Clearly, however, not everything a physician does constitutes treatment, but only those of his interventions that are believed to be helpful or effective against the illness from which the patient suffers; and, among these, only those interventions to which the patient, assuming him to be a conscious adult, consents. In a free society, the fact that a person has an illness or that an illness is attributed to him—regardless of whether the illness is bodily or mental, literal or metaphorical—does not, and cannot, by itself justify imposing medical treatment on him against his will.

Thus, the quarantining of patients with certain contagious diseases has been justified, and can be justified, only by society's right to protect itself from the patient's illness; it cannot be justified by society's right to protect the patient from the consequences of his illness.

It is sometimes claimed that, like patients with contagious diseases, some patients with so-called mental diseases also "endanger society". The precise meaning and the factual validity of this claim are doubtful at best, and the use to which it is put, to justify the necessity of involuntary psychiatric interventions, is illogical and immoral. For if and when "mental patients" endanger or injure others, they do so not through their "illness" but through their behaviour. That this is so is self-evident: it is inherent in our very ideas of contagious and mental diseases. Contagious diseases, such as syphilis or tuberculosis, are things that not only patients can have, but also corpses; whereas mental diseases, such as depression or psychopathy, are things that corpses assuredly can never have. Hence, if and insofar as it is deemed that "mental patients" endanger society, society can, and ought to, protect itself from the "mentally ill" in the same way as it does from the "mentally healthy"—that is, by means of the criminal law. To be sure, society cannot do so as long as it recognizes "mental illness" as both an incriminating condition (as in involuntary hospitalization), and an excusing condition (as in the insanity defence and verdict).

In short, one of the fundamental moral and political implications of the views I have presented here is that one of our most important and most precious rights, and at present one of the most threatened, is the right to be ill—that is, the right to reject treatment, the right to suffer, and the right to die unmolested by interventions imposed upon us by the state acting through its medical (or psychiatric) agencies. In a theological society, we could not sin or die without the cleric, whether we wanted him or not. *Mutatis mutandis*, in a therapeutic society such as ours, we cannot be sick or die without the clinician, whether we want him or not^{8,9}.

British Examples

Lest it be thought that these considerations apply only to psychiatric conditions and practices in the United States, I should like to conclude by calling attention to several recent cases reported in the British press.

First, there are the three women who had been incarcerated in psychiatric institutions for fifty years because of illegitimate pregnancies¹⁰⁻¹³. Perhaps it will be objected that that was long ago, and that such things no longer happen today. Of course not. Today women are hospitalized involuntarily not for having illegitimate babies, but for having illegitimate ideas, which we conveniently call "delusions".

Second, there is the Jordanian eye doctor, the son of the Grand Mufti of Jerusalem, who was accused of killing three children, was promptly found "unfit to plead", and was "detained in a hospital"¹⁴⁻¹⁶.

And third, there is the case of Graham Young, tried only a few months ago, who, having been "cured" at Broadmoor of the disease of enjoying poisoning people, had an unfortunate relapse and poisoned several more¹⁷⁻²⁰. Revealingly, his last bout of evil, though phenomenologically undistinguishable from his previous one, was not attributed to mental disease: this time he was sent to prison, not to Broadmoor. It is difficult to imagine a more clear-cut illustration of one of my basic propositions—namely, that what we call mental illness (especially in a legal context) is not a condition, but a policy; not a fact, but a strategy; in short, not a disease that the alleged patient has, but a decision we make about how to act toward him, whether he likes it or not.

I submit that each of these cases demonstrates an insistent denial of the differences between disease and deviance; between healing for the benefit of the suffering patient and social control for the protection of society; and between medical institutions whose clients are at liberty, because they are free adults, to leave the premises should they be dissatisfied with the service, and penal institutions whose inmates, because they are convicted offenders, are deliberately and explicitly deprived of this option.

What, then, is to be done? A few simple things; however, because of our intense devotion to the medical perspective on human problems, these may prove to be quite unpalatable.

First, as so-called mental health problems are not medical but human (that is, moral, social, and political) problems, we cannot solve them by therapeutic means; we must stop continuing and even intensifying our efforts to solve them by such means.

Second, since the vocabulary of psychiatry serves to re-define systematically moral and political problems as diseases, we must repudiate and stop this abuse of our language.

Third, as psychiatric "treatments" are chiefly overtly or covertly involuntary, such interventions must be disavowed; we must reject the use of psychiatrists as policemen, judges and jailers; and we must seriously dedicate ourselves to the proposition that "mental health" workers should help only those who want to be helped, that they should do so only in ways acceptable to their clients, and that they should stop doing everything else.

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The Synthetic Chemical Literature from 1960 to 1969

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The literature of synthetic chemistry is growing at a rate of 8.7% a year—that is, doubling every 8.3 years. Data on 1.2 million compounds based on more than 128,000 abstracts published in *Index Chemicus* have been analysed. The articles abstracted contain 9.2 new compounds on average.

Current Abstracts of Chemistry and Index Chemicus is a weekly abstracting service covering published journal articles reporting primarily new chemical compounds, new reactions or new syntheses^{1,2}. *Index Chemicus* (IC) was started in June 1960. Originally a monthly publication, IC became a biweekly in 1961 and a weekly in 1967. During the period of the study reported here, 1960 to 1969, all articles containing new inorganic as well as organic compounds were abstracted. The fundamental criteria for a "new" compound are, however, the author's claim of novelty, lack of a reference indicating previous publication of the compound, and therefore the presumption of novelty as for many intermediates.

This ten-year census updates an earlier five-year report³. It is not based on sampling. Rather, precise records have been kept for each journal. The number of articles abstracted and new compounds indexed for the calendar years 1960 to 1969 are shown in Table 1. The number of papers published each year almost tripled during this ten-year period. The first-year growth is atypical because the number of journals covered was then growing rapidly. Growth in subsequent years averaged 8.7%.

The number of compounds per abstract has stayed and remains remarkably steady at an average of 9.2 compounds an article.

By the end of 1969, records were abstracted of more than 1.2 million new compounds. By the end of the Second World War, there were approximately 1 million known chemical compounds in existence, so the new compounds reported between 1960 and 1969 are more than in the entire history of chemistry up to the end of the war. Between 1945 and 1959 another 1 million compounds were reported.

Table 2 shows the percentage of articles published in six of the chief scientific languages—English, German, Russian, French, Japanese and Italian. Ukrainian is included under the heading Russian. "Others" include Spanish, Czech, Hungarian, Polish, Rumanian and so on.

English, as the leading scientific language, has steadily been gaining in strength from 50% of the total output in 1960 to more than 61% in 1969. German, which was formerly the leading scientific language of chemistry, diminished from 17% to 10% during the same period. This does not mean a decline in scientific output by German scientists. On the contrary, the growth of research elsewhere as well as the increased use

Table 1 Compound/Abstract Ratios

Year	Abstracts	Compounds	Compounds/abstract	Increase in No. of abstracts % yr ⁻¹
1960	7,581	70,408	9.3	
1961	9,167	87,496	9.5	
1962	9,899	94,172	9.5	7.4
1963	10,838	100,623	9.3	9.5
1964	12,084	110,230	9.1	11.5
1965	12,824	119,217	9.3	6.1
1966	13,943	128,830	9.3	8.7
1967	15,275	137,245	9.0	8.1
1968	17,830	167,340	9.3	10.1
1969	19,285	172,793	8.9	8.1
Totals	128,726	1,188,354	9.2	8.7
			(average)	(average)

Table 2 Language Distribution 1960-1969

Language	1960		1961		1962		1963		1964		1965		1966		1967		1968		1969	
	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C
English	49.9	49.4	53.0	53.3	52.1	50.9	53.8	52.5	55.5	51.5	55.2	54.6	56.0	54.0	56.9	55.5	61.3	59.7	61.4	60.2
German	16.9	18.7	16.4	18.8	16.2	18.3	16.5	19.1	15.9	18.7	16.4	17.4	15.3	17.4	13.8	15.4	11.8	13.5	10.0	12.6
Russian	14.7	13.1	16.0	12.6	16.4	13.3	16.2	13.4	16.8	14.7	16.4	14.4	16.4	13.9	16.4	14.0	15.4	12.5	17.4	13.8
French	7.5	8.6	5.2	6.1	5.8	7.3	6.0	7.2	4.8	6.9	5.9	7.1	5.5	7.6	6.2	8.3	5.7	7.4	5.9	7.2
Japanese	7.0	6.2	5.7	5.3	6.5	6.0	3.5	3.2	3.1	3.6	3.0	3.1	2.9	3.4	3.1	3.4	2.3	2.9	2.9	3.0
Italian	2.4	2.9	2.0	2.6	2.0	2.6	2.4	3.4	2.1	2.9	1.8	2.3	1.7	1.9	1.9	2.3	1.6	2.2	1.1	1.6
Others	1.6	1.1	1.7	1.3	1.9	1.6	1.6	1.2	1.8	1.7	1.3	1.2	1.9	1.9	1.6	1.3	1.9	1.8	1.5	1.2

A, abstracts; C, compounds.

of English has reduced the percentage, although there was a larger number of abstracts. The same is true of Japanese, which decreased from 7% in 1960 to 2.9% in 1969 during the most spectacular period of growth in the history of Japanese industry. There are many Japanese journals published today in English, and those journals published in Japanese have extensive English summaries.

This same trend also prevails in the languages of other smaller countries—there are very few scientific articles published in Hebrew and Arabic, for example. Almost all papers from developing countries are published in English. A large percentage of Latin American papers appear in English-language journals.

This same trend is not true for articles published in the Soviet Union. Soviet scientists publish overwhelmingly in Russian with the exception of a relatively small number of articles which appear in multilingual international journals, such as *Tetrahedron*, *Tetrahedron Letters* or *The Collection of Czechoslovak Chemical Communications*. In these cases, Soviet scientists publish their work in English, German or French. Soviet chemical publishers are also still quite resistant to the idea of publishing English language summaries. In

general, however, there has been practically no change in the percentage of Russian language publications during the past ten years. The average of 16%, although much lower than figures reported by *Chemical Abstracts* (18.4%)⁴ for all fields of chemistry, is still high by comparison with Western countries. This is in part a consequence of the emphasis in the United States on physical organic rather than synthetic organic chemistry research.

Analysis by Journals

Table 3 shows the sixty top-ranking journals, as far as new chemical compounds are concerned, for 1969. It is interesting to note that eleven of the highest yielding twenty journals are published in English, and these accounted for 75% of the compounds. While many older well-established journals like the *Berichte*, *Annalen*, *Journal of the American Chemical Society*, and *Helvetica* have remained fairly stable, others like *Bull. Soc. Chim. France* have doubled in content as have the Japanese journals published in English. But the newly-established journals like *Tetrahedron Letters* and *Journal of Medi-*

Table 3 Number of New Compounds Reported in 1969

Rank	Journal title	No. of compounds	Rank	Journal title	No. of compounds	Rank	Journal title	No. of compounds
1	<i>J. Chem. Soc. (A, B, C)</i>	11,811	21	<i>Helv. Chim. Acta</i>	2,530	41	<i>Gazz. Chim. Ital.</i>	1,033
2	<i>J. Org. Chem.</i>	9,682	22	<i>Inorg. Chem.</i>	2,349	42	<i>Farmaco Ed. Sci.</i>	1,029
3	<i>J. Med. Chem.</i>	7,775	23	<i>J. Organometallic Chem.</i>	1,981	43	<i>Z. Anorg. Allgem. Chem.</i>	1,024
4	<i>J. Amer. Chem. Soc.</i>	7,638	24	<i>J. Heterocyclic Chem.</i>	1,954	44	<i>Roczniki Chem.</i>	1,001
5	<i>Bull. Soc. Chim. Fr.</i>	6,486	25	<i>J. Prakt. Chem.</i>	1,912	45	<i>Khim. Farm. Zh.</i>	997
6	<i>Tetrahedron Lett.</i>	6,272	26	<i>Austral. J. Chem.</i>	1,841	46	<i>Dokl. Akad. Nauk. SSSR</i>	961
7	<i>Chem. Ber.</i>	5,829	27	<i>J. Inorg. Nucl. Chem.</i>	1,723	47	<i>Arch. Pharmaz.</i>	945
8	<i>Tetrahedron</i>	5,525	28	<i>Arm. Khim. Zhur.</i>	1,575	48	<i>Arzneimittel-Forsch.</i>	900
9	<i>J. Chem. Soc. D Chem. Commun.</i>	5,415	29	<i>Zhur. Neorg. Khim.</i>	1,570	49	<i>Z. Naturforsch. B</i>	893
10	<i>Zh. Obshch. Khim.</i>	4,965	30	<i>J. Indian Chem. Soc.</i>	1,475	50	<i>Carbohyd. Res.</i>	769
11	<i>Zh. Org. Khim.</i>	4,398	31	<i>Acta Chem. Scand.</i>	1,407	51	<i>J. Chem. Soc. Jap. Pure</i>	751
12	<i>CR Acad. Sci. C.</i>	3,837	32	<i>Coll. Czech. Chem. Commun.</i>	1,407	52	<i>Ukr. Khim. Zhur.</i>	728
13	<i>Chem. Pharm. Bull. Jap.</i>	3,777	33	<i>Rec. Trav. Chim.</i>	1,259	53	<i>Biochemistry</i>	714
14	<i>Ann. Chem. Liebigs</i>	3,721	34	<i>Chim. Ther.</i>	1,151	54	<i>Rev. Roumaine Chim.</i>	684
15	<i>J. Pharm. Soc. Jap.</i>	3,195	35	<i>J. Pharm. Sci.</i>	1,123	55	<i>Khim. Prirodnikh. Soed.</i>	669
16	<i>Khim. Geterots. Soed.</i>	3,041	36	<i>Makromol. Chem.</i>	1,103	56	<i>Agr. Biol. Chem.</i>	662
17	<i>Canad. J. Chem.</i>	2,913	37	<i>J. Polymer Sci. A-1</i>	1,085	57	<i>Vysokomol. Soed. A</i>	660
18	<i>Indian J. Chem.</i>	2,806	38	<i>Angew. Chem.</i>	1,061	58	<i>J. Chromatog.</i>	646
19	<i>Bull. Chem. Soc. Jap.</i>	2,745	39	<i>J. Chem. Soc. Jap. Ind.</i>	1,060	59	<i>J. Agr. Food Chem.</i>	639
20	<i>Izvest Akad. Nauk. SSSR Khim.</i>	2,579	40	<i>Z. Chemie</i>	1,041	60	<i>Acta Chim. Acad. Sci. Hung.</i>	638
		104,410			30,607			16,343

cial Chemistry have shown enormous growth—seven-fold and 4.5-fold, respectively.

Rapid communication journals have become very important. In 1960, the *Proceedings of the Chemical Society* contained 301 new compounds. By the time it changed its name to *Journal of the Chemical Society, Part D, Chemical Communications* in 1965, it contained 1,527 compounds a year, a five-fold increase, only to show a 3.6-fold increase by 1969 in which year it contained 5,415 compounds. In the same ten-year period, the yearly number of new compounds reported in *Tetrahedron Letters* increased from 876 to 6,272.

The output in the Soviet literature has grown considerably. Output for *Zhurnal Obshchei Khimii* grew steadily between 1960 and 1964, when it suddenly dropped off. This coincided with the publication of *Zhurnal Organicheskoi Khimii* and *Khimiya Geterotsiklicheskikh Soedinenii*. The combined output of these three journals increased by 100% during those years.

As shown in Table 3, analysis of journals by rank (in terms of yield of new compounds) shows that journals of rank 1 to 20 yield almost two-thirds of all compounds. Data are taken from the calendar year of 1969 but are also representative of other years.

Bradford's Law

According to Bradford's law⁵ (illustrated in Fig. 1), one generally observes that a large part of the information in a specialized field can be obtained from a few top-ranking journals in that field. As the number of journals examined grows, the information gathered diminishes exponentially. In the case of synthetic chemistry, only seven journals were required to account for one-third of the compounds indexed in 1969. Only twenty-seven journals were required to cover two-thirds. More than 2,000 were needed to produce the last one-third. It is, however, more realistic to say that 158 journals account for the balance. In fact, 96% of the total output for 1969 was contained in only 100 journals. The dominance of a small key group of journals is much more dramatic in synthetic chemistry than that implied by a previous study⁶, which reported that about 1,000 journals must be scanned to obtain 80% to 90% of the "chemical" literature reported in *Chemical Abstracts*. The IC census data correspond more closely to citation studies based on the *Science Citation Index* where it is found that the same small group of journals accounts for 90% or more of the citations appearing in chemical and other journals⁷⁻⁹.

To support this finding to our own satisfaction, a separate study was conducted from 1967 to 1969 to make sure that no important chemical journals was overlooked. Article titles from 2,000 additional journals were searched by computer using ISI's Automatic Subject Citation Alert (ASCA). The project was discontinued when it became clear that these 2,000 journals only contributed 1% of the output obtained from less than 200 journals. As these journals were all covered in the *Science Citation Index*, the probability that pertinent information would be lost in a comprehensive literature search is very low indeed. Any cost-sensitive approach to information management must set some upper limit on the scope of any service¹⁰.

Duplication for Searchers

The chief conclusions of our study are as follows. First, the synthetic chemical literature has been growing steadily at a rate of approximately 8.7% a year; second, English is increasingly the leading language of chemical communication and about two-thirds of the newly prepared compounds are re-

ported in English; third, one-third of all new chemical compounds are published in seven primary journals, half in fifteen, two-thirds in twenty-five; only 100 are needed to cover 96%.

As far as new synthetic chemistry is concerned, a cost effective service is provided by examining a carefully chosen

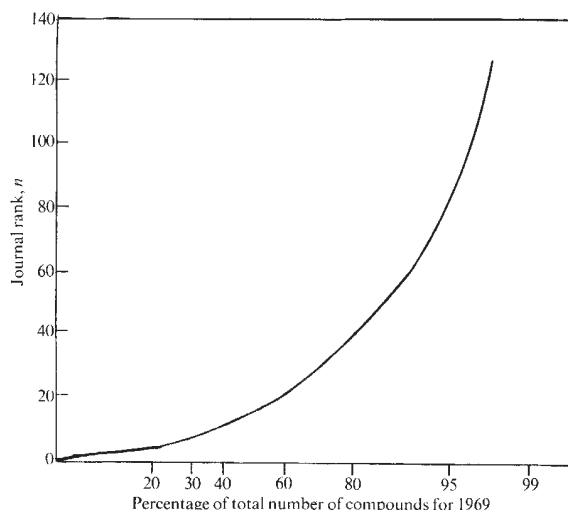


Fig. 1 Percentage of total number of compounds reported in 1969 for journals of rank $< n$. For $n=1-20$, the number of compounds is 104,361; for 21-40, 30,656; for 41-60, 16,343; for 61-80, 7,154; for 81-100, 5,238; for 101-183, 7,041.

and monitored list of 100 to 200 key journals. Although there may be other justifications for monitoring 12,000 journals at *Chemical Abstracts*⁴, it certainly cannot be justified for the needs of synthetic chemistry.

Limitations

It may be argued that additional new compounds are found as a consequence of abstracting for other branches of chemistry, but there are economic limitations involved when one considers the exponential increase in computer and other costs involved if one must check all compounds, new and old, through a large-scale registry. Furthermore, the more intensive line by line examination and indexing of the more significant articles in synthetic chemistry, by contrast with indexing from abstracts, produces a number of not otherwise reported compounds, including thousands of intermediates.

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² Revesz, G. S., and Warner, A., *J. Chem. Doc.*, **9**, 106 (1969).

³ Garfield, E., and Foeman, G., *American Chemical Society 148th Meeting, Abstract*, No. G31 (September 1964).

⁴ Baker, D. B., *Chem. Eng. News*, **49** (28), 36 (1971).

⁵ Bradford, S. C., *Documentation* (Crosby Lockwood, London, 1948).

⁶ Wood, J. L., *The Parameters of Document Acquisition at Chemical Abstracts Service, American University Eighth Annual Institute of Information Storage and Retrieval* (Washington, DC, February 14-17, 1966).

⁷ Garfield, E., *Science* (in the press).

⁸ Garfield, E., *Current Contents*, No. 5, 6 (February 2, 1972).

⁹ Garfield, E., *Current Contents*, No. 9, 5 (March 1, 1972).

¹⁰ Weinstock, M., *Nature*, **233**, 434 (1971).

Five-Year Climatic Trend for the Northern Hemisphere

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Between May 1958 and April 1963 the mean temperature of the atmosphere in the northern hemisphere fell by about 0.60° C. The data which lead to this conclusion are presented in this article.

LARGELY as a result of possible man-made environmental effects, there attaches much interest at present to the study of observed climatic trends¹. These trends may relate to regional conditions, or to the mean state of the entire atmosphere over one hemisphere or even over the whole Earth. Many studies of the latter two types have been made, usually from surface meteorological measurements²⁻⁴. These generally carry the lingering suspicion that perhaps the data used are too limited in space, chiefly vertically, to give a representative measure of conditions for, say, the air in the northern hemisphere as a whole. In order to improve this situation we have therefore computed, among certain other things, the mean temperature and water vapour content for the atmosphere in the northern hemisphere up to 75 mbar (about 18 km above sea level) by months from all available daily meteorological soundings during the five-year period which started on May 1, 1958. The mode of computing was such as to give the mass averages of the temperature and vapour content.

Treatment of Data

The data collection used comprises the so-called MIT General Circulation Data Library, which was compiled several years ago chiefly for the study of the dynamics of the atmosphere. It is the most refined and complete accumulation of daily meteorological data for the northern hemisphere, in convenient form for research purposes, now in existence. Its preparation,

checking and trial applications required a few years of labour. The total number of once a day (00Z) upper-air observing stations used was about 600 of which about 300 on the average reported useful measurements up to at least 500 mbar each day.

As the station network is irregular geographically, it was necessary to interpolate horizontally to secure values of the required quantities at regular gridpoints of a latitude-longitude net. This was done by objective computer analysis of the hemispheric data at each level according to a scheme devised by Oort and Rasmusson⁵. The temperature and humidity fields were thus analysed by months at the 1,000, 950, 900, 850, 700, 500, 400, 300, 200, 100 and 50 mbar levels. A few southern hemisphere equatorial stations were used in the analyses to help provide more accurate values in the tropics. From these analyses the vertical average temperature and specific humidity with respect to pressure were computed at each gridpoint for each month from the surface to the 75 mbar level. As the atmosphere is in close hydrostatic equilibrium, these vertical means constitute vertical mass averages.

The vertical averages were then integrated geographically, with proper mass weighting for each gridpoint, over the entire hemisphere or subregion of it. The hemispheric integration thus yielded sixty mass-average monthly values of the temperature and sixty more of the humidity for the atmosphere below the 75 mbar level. This upper limit implies that a little more than 92% of the atmosphere was included in the computations. Each monthly mean temperature is based on about 150,000 to 200,000 measured temperatures.

Our principal purpose here is to present the set of numbers which were obtained by the process outlined. It will thus be possible for those who so desire to analyse the material for the presence of a trend in such manner as they think proper, statistically or otherwise, or by combining it with other information to achieve other aims. As a simple example, however, we also present below our own trial analysis, possibly to serve as a basis for future discussion and to bring out certain further aspects of our data.

Table 1 Monthly Mean Hemispheric Mass-average Temperatures and Humidities for the Atmosphere between 0° N and 90° N

	1958-1959		1959-1960		1960-1961		1961-1962		1962-1963		Mean seasonal cycle	
	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity
May	-15.58	3.05	-15.74	3.03	-15.79	3.07	-15.70	2.99	-16.33	3.02	-15.82	3.03
June	-13.54	3.53	-13.68	3.44	-13.69	3.46	-13.76	3.42	-14.21	3.34	-13.78	3.44
July	-12.31	3.83	-12.50	3.81	-12.54	3.84	-12.61	3.78	-12.94	3.71	-12.58	3.79
Aug.	-12.67	3.83	-12.64	3.83	-12.40	3.90	-12.79	3.82	-13.22	3.65	-12.74	3.80
Sept.	-14.24	3.51	-14.17	3.55	-14.33	3.54	-14.37	3.46	-14.62	3.44	-14.34	3.50
Oct.	-16.43	3.10	-16.47	3.06	-16.67	3.03	-16.83	3.02	-16.77	3.04	-16.63	3.05
Nov.	-18.66	2.71	-18.57	2.64	-18.86	2.63	-18.96	2.61	-18.96	2.65	-18.80	2.65
Dec.	-20.06	2.39	-20.00	2.37	-19.91	2.37	-20.51	2.31	-20.46	2.39	-20.19	2.37
Jan.	-20.49	2.19	-20.65	2.16	-20.72	2.16	-20.93	2.11	-21.13	2.19	-20.78	2.16
Feb.	-20.80	2.14	-20.50	2.18	-20.81	2.16	-20.71	2.13	-20.96	2.15	-20.76	2.15
March	-19.51	2.26	-20.18	2.32	-19.95	2.31	-20.09	2.33	-20.35	2.21	-20.02	2.28
April	-17.68	2.62	-18.12	2.65	-17.97	2.58	-18.30	2.55	-18.35	2.58	-18.08	2.59
Annual mean	-16.81	2.93	-16.94	2.92	-16.97	2.92	-17.13	2.88	-17.36	2.86	-17.04	2.90

The temperatures are in °C and the (specific) humidities are in g of water vapour kg⁻¹ moist air.

Monthly Means

Table 1 shows the sixty values of the hemispheric mean temperature. Table 1 also contains the corresponding sixty hemispheric mean specific humidity values. Table 2 lists sixty monthly mean temperatures and humidities similar to those in Table 1, but averaged over the complete zonal belt between the equator and 30° N. Table 3 gives similar mean temperatures and humidities but averaged over the remaining half of the hemisphere, that is from 30° N to the pole.

In our own sample analysis of the material the following procedure was used. It is clear that the data in Table 1 show a strong seasonal cyclic character. To investigate this property, a Fourier series of thirty terms was fitted to the sixty values. These are given in Table 4. As might be expected, the annual and semi-annual Fourier cycles have the largest amplitudes. The higher harmonics of the yearly variation, namely the 4, 3 and 2 month cycles, are smaller. As these five components could lead to a spurious trend for the five year period, they were in effect removed from the original numbers by subtracting the mean seasonal cycle. A graph of the temperature residuals is shown in Fig. 1a. As expected, all the seasonal cyclic components are absent, and the remaining variance is quite small. It is apparent by eye that the curve has a trend toward lower temperatures as the five-year period advances. To estimate this trend more objectively a linear trend line was fitted to the residuals by least-square methods (dashed line in Fig. 1a). It seems that there is a trend in the data toward decreasing temperature over the northern hemisphere of approximately 0.60° C (about 1.1° F) during the five-year period. The hemispheric humidity residuals computed in like fashion are depicted in Fig. 1d. They show a decrease of about 0.08 g of vapour kg⁻¹ of (moist) air, again as computed from a linear trend line.

Figure 1b is analogous to Fig. 1a, save that it depicts the

temperatures calculated for the belt between the equator and 30° N. The temperature trend in this case gives a cooling of about 0.81° C. Fig. 1c is again similar to Fig. 1a but shows the trend for the polar cap (30° N to 90° N). The cooling is 0.39° C. Fig. 1e shows the humidity residuals for the belt from 0° N to 30° N which give a linear decreasing trend of 0.10 g kg⁻¹. Finally, Fig. 1f gives the humidity residuals for the polar cap north of 30° N and shows a decreasing linear trend of 0.07 g kg⁻¹ for the five years.

As an objective test of significance of the computed linear trends, we have computed 95% confidence intervals according to a method described by Kendall and Stuart⁶. Using their formula (28.93) we evaluated the confidence limits at the beginning (CI₁) and in the middle (CI₃₀) of the series. The resulting values are also shown in Fig. 1; they indicate the significance of the computed trends, at least as they apply during the five-year period.

The remaining three Figures show the contribution from different segments of the atmosphere to the integrated hemispheric trend. The first (Fig. 2) gives the five-year trend in the zonal mean temperature (that is, the temperature averaged with respect to longitude) for different levels and latitudes. We find strong cooling both in the subtropics and at very high latitudes. The cooling in the subtropics, however, dominates the hemispheric trend because it represents typical conditions over a larger area. There are some regions of computed heating, but they are of small magnitude and extent. They are chiefly located close to the Earth's surface, where the net hemispheric trend practically vanishes.

The contribution from different geographical regions to the hemispheric trend is shown in Fig. 3. In constructing this figure, the trend in vertical mean temperature was computed for each point of a 47 by 51 grid covering the hemisphere. The largest cooling rates are again found in the subtropics with

Table 2 Monthly Mean Mass-average Temperatures and Humidities for the Atmosphere between 0° N and 30° N

	1958-1959		1959-1960		1960-1961		1961-1962		1962-1963		Mean seasonal cycle	
	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity
May	-10.33	4.43	-10.82	4.37	-10.80	4.45	-10.91	4.31	-11.32	4.40	-10.84	4.39
June	-10.03	4.77	-10.27	4.59	-10.27	4.62	-10.74	4.54	-11.02	4.45	-10.46	4.59
July	-10.09	4.83	-10.55	4.75	-10.54	4.84	-10.78	4.73	-10.81	4.68	-10.55	4.76
Aug.	-10.27	4.87	-10.44	4.80	-10.03	4.98	-10.43	4.84	-10.96	4.65	-10.43	4.83
Sept.	-10.25	4.76	-10.36	4.81	-10.54	4.83	-10.75	4.68	-10.71	4.73	-10.52	4.76
Oct.	-10.86	4.51	-10.88	4.46	-11.11	4.45	-11.49	4.38	-11.30	4.43	-11.13	4.45
Nov.	-11.60	4.14	-11.57	4.01	-11.69	4.04	-12.19	3.95	-12.15	4.05	-11.84	4.04
Dec.	-12.23	3.71	-12.01	3.69	-12.19	3.73	-12.45	3.59	-12.66	3.75	-12.31	3.68
Jan.	-12.31	3.42	-12.41	3.37	-12.41	3.40	-12.46	3.29	-13.02	3.44	-12.52	3.38
Feb.	-12.46	3.37	-12.27	3.35	-12.69	3.38	-12.54	3.33	-13.17	3.41	-12.65	3.37
March	-11.80	3.49	-12.23	3.64	-12.21	3.62	-12.50	3.65	-12.68	3.47	-12.28	3.57
April	-11.34	3.94	-11.49	4.09	-11.68	3.91	-11.91	3.89	-11.93	3.93	-11.67	3.95
Annual mean	-11.13	4.19	-11.28	4.16	-11.35	4.19	-11.60	4.10	-11.81	4.12	-11.43	4.15

The temperatures are in °C and the (specific) humidities are in g of water vapour kg⁻¹ moist air.

Table 3 Monthly Mean Mass-average Temperatures and Humidities for the Atmosphere between 30° N and 90° N

	1958-1959		1959-1960		1960-1961		1961-1962		1962-1963		Mean seasonal cycle	
	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity	Temperature	Humidity
May	-20.82	1.67	-20.66	1.70	-20.78	1.69	-20.49	1.68	-21.34	1.64	-20.82	1.69
June	-17.06	2.28	-17.10	2.29	-17.10	2.29	-16.77	2.30	-17.40	2.23	-17.08	2.28
July	-14.53	2.84	-14.45	2.87	-14.55	2.84	-14.43	2.83	-15.06	2.74	-14.60	2.82
Aug.	-15.07	2.79	-14.83	2.87	-14.77	2.83	-15.14	2.79	-15.47	2.66	-15.06	2.79
Sept.	-18.24	2.25	-17.98	2.29	-18.12	2.25	-18.00	2.24	-18.54	2.14	-18.16	2.23
Oct.	-22.00	1.69	-22.06	1.67	-22.22	1.60	-22.17	1.66	-22.24	1.65	-22.14	1.65
Nov.	-25.73	1.28	-25.57	1.27	-26.02	1.22	-25.73	1.27	-25.77	1.25	-25.76	1.26
Dec.	-27.89	1.07	-27.98	1.05	-27.62	1.00	-28.57	1.04	-28.26	1.02	-28.06	1.04
Jan.	-28.68	0.96	-28.89	0.95	-29.03	0.92	-29.40	0.92	-29.24	0.94	-29.05	0.94
Feb.	-29.15	0.91	-28.73	1.01	-28.93	0.94	-28.87	0.92	-28.75	0.90	-28.88	0.94
March	-27.22	1.03	-28.14	1.00	-27.68	1.01	-27.67	1.01	-28.02	0.95	-27.75	1.00
April	-24.01	1.29	-24.75	1.22	-24.25	1.26	-24.68	1.21	-24.78	1.23	-24.49	1.24
Annual mean	-22.53	1.67	-22.60	1.68	-22.59	1.65	-22.66	1.66	-22.91	1.61	-22.65	1.65

The temperatures are in °C and the (specific) humidities are in g of water vapour kg⁻¹ moist air.

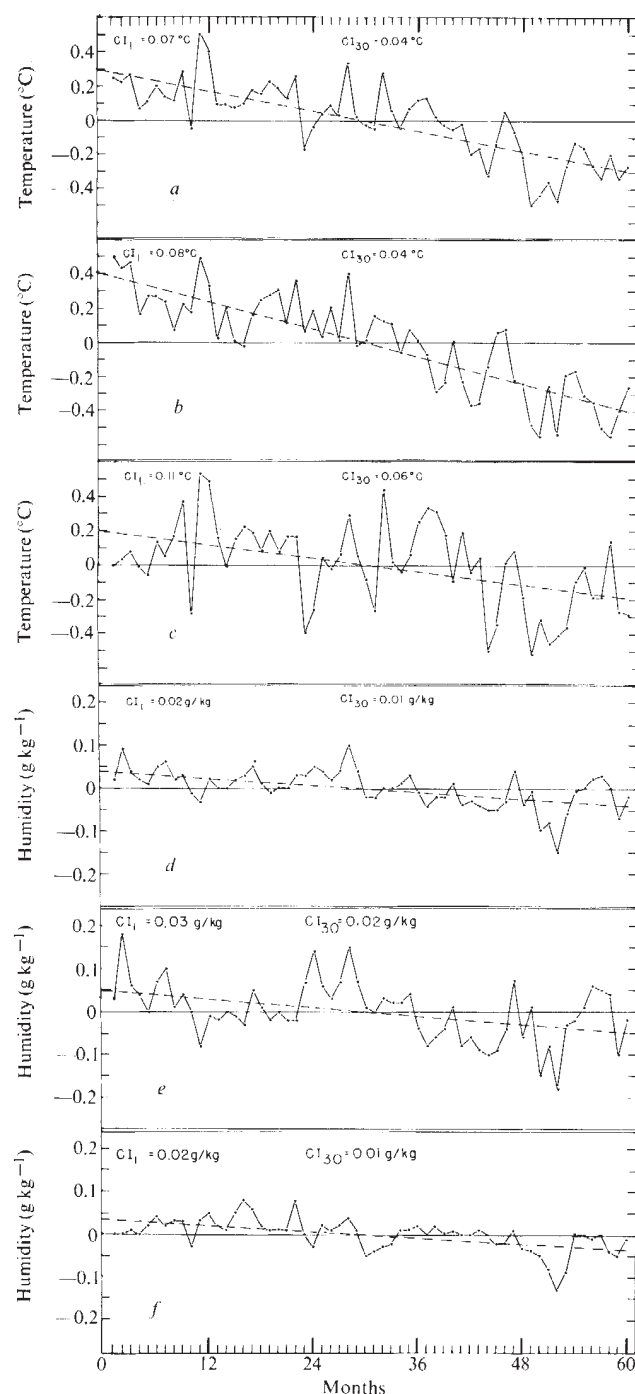


Fig. 1 Monthly mean mass-average values for the period May 1958 to April 1963. *a*, Hemispheric mean temperature; *b*, mean temperature 0° N to 30° N; *c*, mean temperature 30° N to 90° N; *d*, hemispheric mean specific humidity; *e*, mean specific humidity 0° N to 30° N; *f*, mean specific humidity 30° N to 90° N. ---, Least-square linear trend lines. As described in the text the annual cycle was removed but otherwise the values are raw and unsmoothed.

maxima over northern Africa and southern Asia. At this point it is relevant to mention the non-uniform character of the distribution of radiosonde stations over the Earth. Most stations are located over land and at middle latitudes. There are large gaps in the network south of about 20° N over the eastern North Pacific and the North Atlantic Ocean. Therefore one cannot fully discount the possibility of some compensating heating effect over part of the tropical oceans, which was overlooked in our analysis. Such a compensation seems unlikely, however, in view of the general cooling tendency over

Table 4 Results of Harmonic Analysis of Series of Monthly Temperature and Specific Humidity Averages over the Entire Northern Hemisphere for the Period May 1958 to April 1963

Period (months)	Temperature		Specific humidity	
	Amplitude ($^{\circ}$ C)	Phase (months)	Amplitude (10^{-3} g kg $^{-1}$)	Phase (months)
60.0	0.21	17.5	34	16.4
30.0	0.12	6.3	19	1.1
20.0	0.02	2.5	14	2.6
15.0	0.03	2.2	5	-1.6
12.0	4.24	2.3	835	2.6
10.0	0.01	3.2	21	-4.8
8.6	0.10	1.8	9	3.5
7.5	0.05	1.5	16	1.7
6.7	0.04	-0.6	20	0.6
6.0	0.37	2.3	85	2.4
5.5	0.01	0.0	14	0.4
5.0	0.07	0.7	9	1.5
4.6	0.01	-1.6	5	0.9
4.3	0.04	1.6	5	1.2
4.0	0.08	-0.2	23	-1.2
3.8	0.04	0.8	14	0.7
3.5	0.05	-0.1	4	-0.5
3.3	0.05	0.6	2	-0.5
3.2	0.02	-1.5	6	-1.2
3.0	0.04	-0.6	8	-0.1
2.9	0.02	-1.0	4	-0.7
2.7	0.03	-0.5	2	-0.1
2.6	0.06	0.0	4	0.6
2.5	0.02	-0.0	4	1.0
2.4	0.01	-0.8	13	-0.3
2.3	0.01	1.1	7	-0.6
2.2	0.01	0.3	10	-1.0
2.1	0.04	-0.6	8	0.9
2.1	0.04	0.0	5	0.5
2.0	0.02	—	2	—

Phase is given as the time of nearest maximum in months following (or preceding) May 15, 1958.

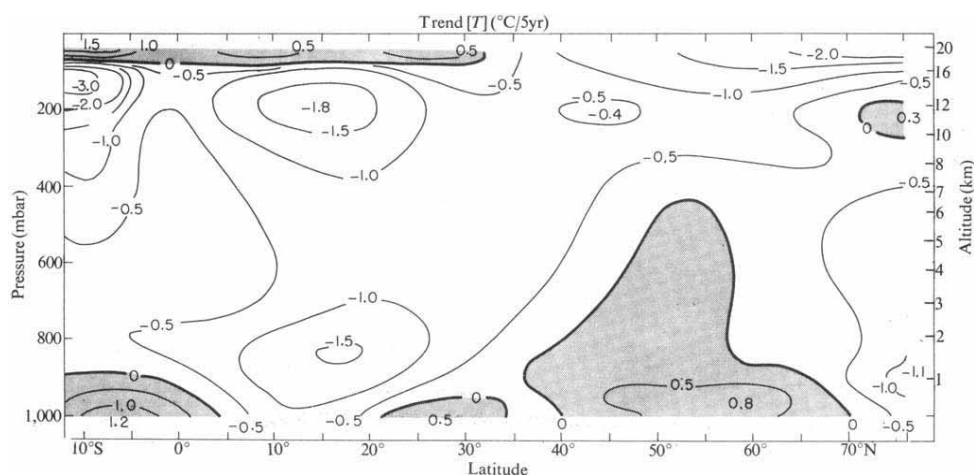
the rest of the map. As a final item, the geographical distribution of the five-year trend in vertical mean humidity is shown in Fig. 4. The pattern is more complex than that of the temperature. In spite of the parallel downward trends in temperature and humidity on a hemispheric scale, the local trends are in some cases of opposite sign (see, for example, over Africa and India). In so far as these features are significant, the explanation of local differences should probably be in terms of an increase or decrease in adiabatic heating or cooling induced by dynamic processes.

Comments and Speculations

One of the first questions one may be inclined to ask is whether the downward trend in temperature and humidity can be extended beyond the five-year period. Past experience with other meteorological time series suggests that such a prediction would most likely lead to erroneous conclusions. Suppose, for example, that the calculated cooling in the northern hemisphere were to continue at the rate of -0.6° C every 5 yr for a century. Then the mean temperature would decrease by 12° C, a value which is clearly unrealistic. Thus, the downward trend in the 1958–1963 sample seems to represent part of a longer term natural fluctuation and probably will not continue in the decade following 1963.

This question clearly indicates the need to keep better track of the Earth's climate by reducing much longer representative data series than were used in the present study. It is indeed strange that—in spite of the extensive monitoring of local weather—one does not know the order of magnitude or even the sign of the changes which undoubtedly take place in the bulk of the atmosphere at the present time. Such knowledge is, of course, a prerequisite before one can assess the mechanisms responsible for climatic change and also the possible impact of man's activities on the climate. Both at the Massachusetts Institute of Technology and at the Geophysical Fluid Dynamics Laboratory of the National Oceanic and Atmospheric Administration projects are under way to extend the sample to after April 1963.

Fig. 2 Latitude-height cross-section of the linear trend in the zonal mean temperature during the period May 1958 to April 1963 ($^{\circ}\text{C}/5\text{ yr}$).



Up to this point we have discussed the situation in the northern hemisphere. In the southern hemisphere, the distribution of upper air stations is quite poor by comparison. Recent developments in measuring vertical temperature profiles from meteorological satellites promise, however, an improvement in the future monitoring of the climate over the entire Earth.

Aside from registering slow changes in the heat content of the atmosphere, it will be important to expand and coordinate efforts to measure changes in heat storage in the other components of the Earth-atmosphere system. For example, the water in the oceans and also the snow and ice in glaciers and in the ice caps can either store or release huge amounts of heat and thereby affect the Earth's climate. In this connexion, it may be of interest to note that since about 1958 there seems to have been a rather uniform trend toward lower values of the surface temperature both in the North Atlantic Ocean^{7,8} and in the North Pacific Ocean⁹.

As to an explanation of the cause or causes of climatic trends such as those presented here, the field is wide open for speculation. First of all, there are astronomical factors involved such as the solar constant, its annual variation and the spectral

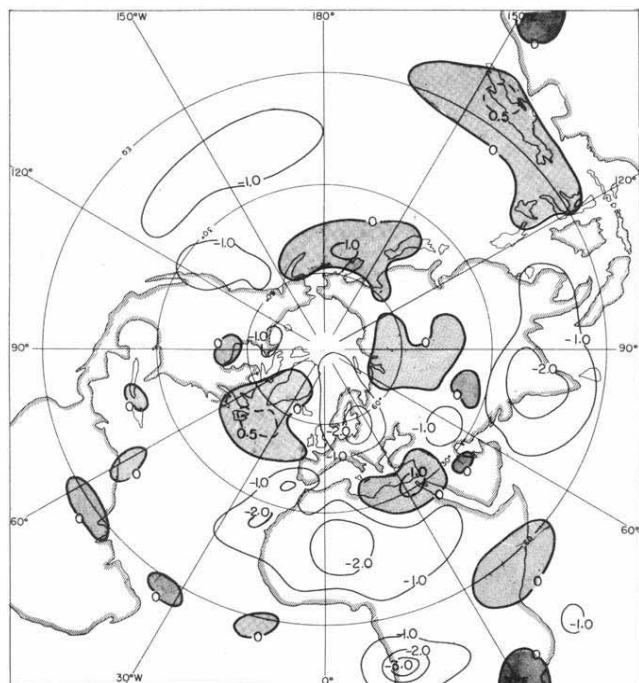


Fig. 3 Geographical distribution of the linear trend in the vertical mean (mass-weighted) temperature during the period May 1958 to April 1963 ($^{\circ}\text{C}/5\text{ yr}$).

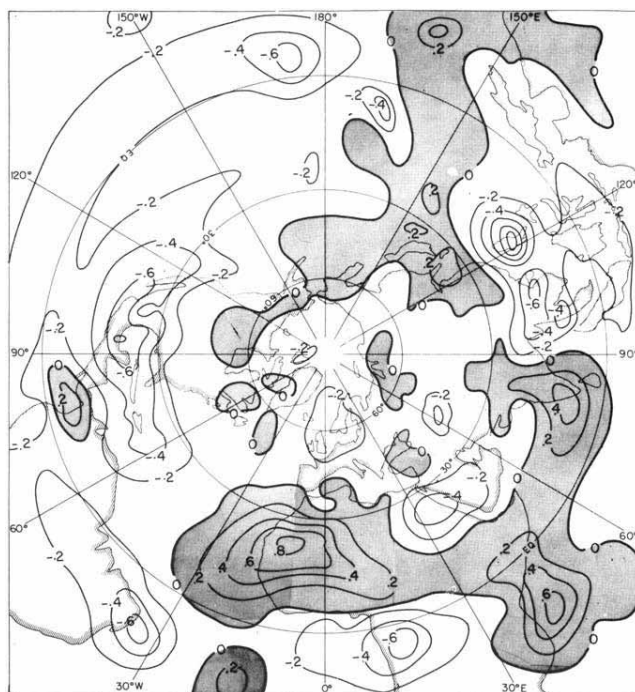


Fig. 4 Geographical distribution of the linear trend in the vertical mean (mass-weighted) specific humidity during the period May 1958 to April 1963 ($\text{g kg}^{-1}/5\text{ yr}$).

distribution of the incoming solar radiation. In addition, there is the possibility of internally generated cycles caused by factors in the atmosphere-ocean-cryosphere system itself. For instance, changes in chemical composition of the atmosphere, changes in albedo of the solid Earth arising from variations in vegetation, snow or ice cover, and changes in temperature of the ocean surface would strongly affect the atmospheric heat balance.

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Reactions between an Insect Picornavirus and Naturally Occurring IgM Antibodies in Several Mammalian Species

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Domestic and wild animals have IgM antibodies which react with insect viruses. Infection by agents sharing common antigens with the insect viruses could account for this phenomenon.

THE USE of viruses to control insect pests is attractive because of the undoubted economic advantage and apparent high degree of specificity. Insect viruses are claimed to have a restricted host range and there are no records of transmission to animals outside the class Insecta. Here, however, we describe serological reactions between a picornavirus which infects *Gonometa podocarpi* (Lepidoptera: Lasiocampidae) and naturally occurring antibodies in several mammalian species, which suggests that the animals may have been exposed to the virus or a serologically related antigen.

Serological Relationships

Gonometa virus is morphologically similar to the small RNA viruses infecting vertebrates and also resembles them in several physico-chemical properties; for example, it contains 37% single-stranded RNA, the protein moiety comprises four polypeptides with molecular weights ranging from 36,500 to 12,000 and the virus has a buoyant density of 1.35 g cm^3 in caesium chloride¹. Tests were therefore made to determine whether any serological relationships existed between the *Gonometa* virus and vertebrate picornaviruses. Bovine enterovirus VG-5-27², porcine enterovirus Italian 1/66³, encephalomyocarditis virus, vesicular exanthema virus and several serotypes of foot-and-mouth disease virus, each of which gave a precipitation line with its homologous antiserum in immunodiffusion tests, did not react with *Gonometa* virus antisera which had been produced in rabbits and guinea-pigs and gave a homologous reaction at a dilution of 1/16. Nor were precipitation lines obtained between the *Gonometa* virus and hyperimmune guinea-pig antisera to the vertebrate viruses listed above.

The chance observation, however, that sera from pigs infected with the Italian 1/66 virus produced a precipitation line with purified *Gonometa* virus prompted a more detailed examination of this reaction. When sera from pigs infected with foot-and-mouth disease were reacted with purified *Gonometa* virus, a precipitation line appeared in each test. This line gave a pattern of non-identity with the line produced

by the same serum and foot-and-mouth disease virus particles but it did fuse with that produced by *Gonometa* virus and its homologous rabbit antiserum (Fig. 1). Moreover, pre-inoculation sera from all the animals subsequently infected with foot-and-mouth disease virus also gave a precipitation line with *Gonometa* virus and all the six sera we examined were strongly positive.

IgM Antibody

The substance in the pig serum giving this reaction was stable at 56°C , but precipitating activity was destroyed when the serum was treated overnight with 0.1 M 2-mercaptoethanol. This suggested that the reaction involved IgM antibody and the following confirmatory evidence has been obtained.

Serum from a pig infected 7 days previously with foot-and-mouth disease virus was centrifuged for 16 h at $90,000g$ in a 15–25% sucrose gradient. Fractions from the gradient were concentrated with half-saturated ammonium sulphate and tested with *Gonometa* virus and foot-and-mouth disease virus. The fractions from the 19S region of the gradient gave a precipitation line with each virus (Fig. 2). Serum from an animal infected some weeks previously was fractionated similarly. The fractions from the 19S region of the gradient with this serum gave a line with *Gonometa* virus and a weak reaction with foot-and-mouth disease virus, whereas the fractions from the 7S region gave a reaction with foot-and-mouth disease virus only.

Serum samples from a pig infected with foot-and-mouth disease virus were electrophoresed in agarose and the separated

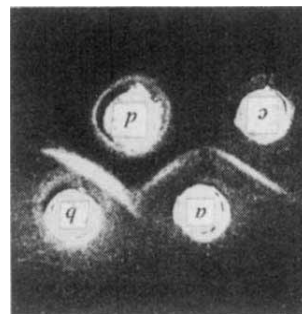


Fig. 1 Immunodiffusion test with *Gonometa* virus (a), foot-and-mouth disease virus (b), rabbit antiserum to *Gonometa* virus (c) and serum from a pig infected with foot-and-mouth disease virus (d). The test shows the identity of the lines produced with *Gonometa* virus and the two sera and the non-identity of the lines produced with the pig serum and the two viruses.

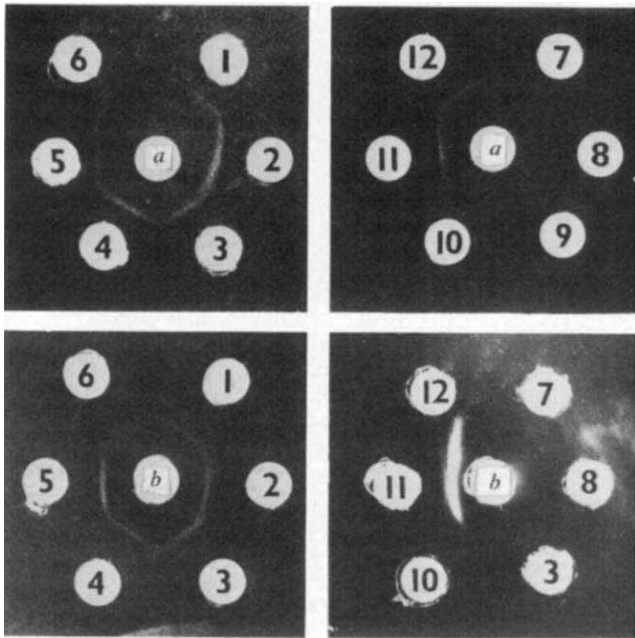


Fig. 2 Immunodiffusion test of the fractions prepared by sucrose gradient centrifugation of pig serum obtained seven days after infection with foot-and-mouth disease virus, using *Gonometa* virus (a) and the homologous foot-and-mouth disease virus (b) as antigens. 1–10 refer to the sucrose gradient fractions, numbered from the bottom of the tube. Unfractionated pig serum and rabbit antiserum to *Gonometa* virus are at positions 11 and 12.

proteins then allowed to diffuse towards channels containing *Gonometa* virus or foot-and-mouth disease virus. Serum taken 7 days post-infection gave a precipitation line with each

virus at the position of IgM. Serum collected 18 days post-infection gave a line with *Gonometa* virus only at the IgM position, whereas the reaction with foot-and-mouth disease virus was mainly at the position of IgG.

Mixtures of *Gonometa* virus and purified IgM antibody from pig serum were examined in the electron microscope. Complexes were observed which were similar to those obtained with foot-and-mouth disease virus and the homologous IgM antibody⁴ and with *Gonometa* virus and its homologous IgM antibody. The complexes of *Gonometa* virus and IgM antibody from pig serum showed attachment of antibody molecules at regular intervals on the virus surface (Fig. 3). In contrast, complexes of *Gonometa* virus with the homologous IgG antibody showed attachment of the antibody molecules over the entire surface of the virus.

The *Gonometa* virus did not react with the IgG fraction prepared by DEAE-cellulose chromatography of serum from pigs infected with foot-and-mouth disease virus. This IgG antibody preparation gave a precipitation line with the homologous virus.

In all the tests described, the *Gonometa* virus particles had been purified by sucrose gradient and caesium chloride centrifugation. The supernatant from the infected insect homogenate, from which the virus had been pelleted at 80,000g, did not give a reaction with the pig serum. This indicated that soluble insect proteins did not react non-specifically with any components of the pig serum. Further, a recently isolated virus from *Darna trima* (Lepidoptera: Limacodidae) (J. S. R. and J. F. L., unpublished data), obtained from Sabah (formerly Borneo), which is not related serologically to the *Gonometa* virus, also gave a precipitation line with the pig serum and this did not fuse with the line produced by *Gonometa* virus (Fig. 4); thus, these reactions are not identical. These observations suggest that the reaction between *Gonometa* virus and pig serum is specific.

Because natural antibodies of the IgM class are found in the sera of a wide range of animals, pig serum giving a strong

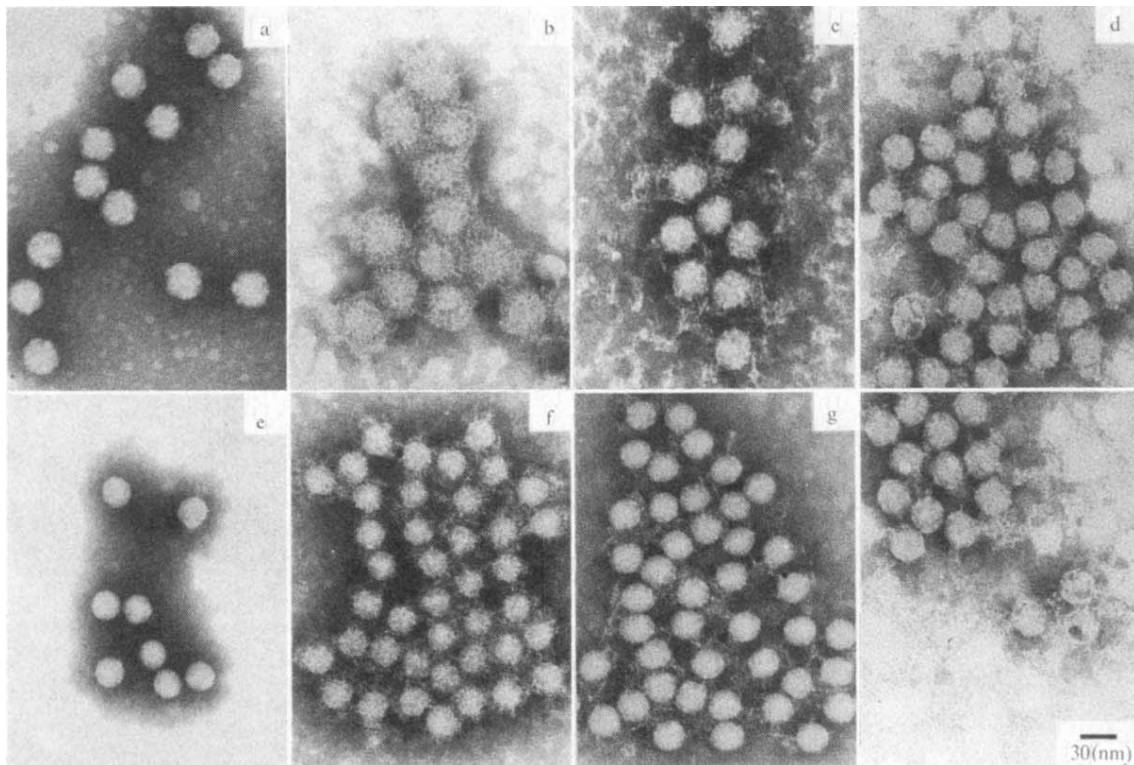


Fig. 3 Electron micrographs of complexes of *Gonometa* virus with the specific IgG and IgM antibodies and with the IgM fraction of pig serum compared with those obtained with foot-and-mouth disease virus and the specific IgG and IgM antibodies: a, *Gonometa* virus alone; b, plus IgG; c, plus IgM; d, plus IgM fraction from pig serum; e, FMDV alone; f, plus IgG; g, plus IgM.

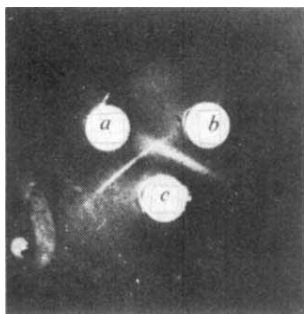


Fig. 4 Immunodiffusion test of *Gonometa* virus (a) and *Darna trima* virus (b) with pig serum (c), showing the lack of identity in the two reactions.

reaction with *Gonometa* virus was tested with a range of bacterial antigens which have been shown to react in some cases with IgM from animals not experimentally exposed to the antigens. Only one of ten antigens, namely *Salmonella minnesota* glycolipid, gave a precipitation reaction with the pig serum and this line did not fuse with that produced by *Gonometa* virus. Furthermore, as antigens on sheep red blood cells react with sera from other species, pig serum which had been absorbed with sheep red blood cells was tested with *Gonometa* and *Darna trima* viruses. The absorbed serum gave a precipitation line with each virus.

Reactions with Other Species

The sera of several other species have also been tested for their reactivity with *Gonometa* virus. Reactions were obtained with sera from cattle (10/10), sheep (4/6), horses (4/6), dogs (1/6) and three species of deer (10/10). The intensity of the reaction varied considerably in individual animals of the same species, for example, some undiluted sera gave only a faint reaction whereas reactions were occasionally obtained with sera diluted 1/8. The precipitation lines obtained with the different species fused, providing further evidence for the specificity of the reaction. No reactions were obtained with sera from guinea-pigs and rabbits which had been reared for laboratory purposes, nor with wild rabbit sera. It was significant that sera obtained from gnotobiotic pigs (6 animals) and cattle (6 animals) did not react with *Gonometa* virus.

These observations raise some important questions, particularly as to the stimulus which produces IgM antibody in these animal species. It is possible that the reaction occurred because the animals had previously been exposed to *Gonometa* virus. As the *Gonometa* virus was isolated from an insect species which is indigenous to East Africa and has not been recorded elsewhere, it seems unlikely that this virus induced the response. The class Insecta contains some 75% of the known animal species, however, of which only a small number have been examined for the viruses they may harbour, and it is quite feasible that the *Gonometa* virus or serologically related viruses occur in other parts of the world. Indeed, in some instances, close serological relationships have been demonstrated between viruses isolated from quite unrelated insects whose habitats are widely separated geographically^{5,6}. It is possible therefore that there are viruses either of invertebrate or of vertebrate origin which are widely prevalent in the United Kingdom which share common antigens with the *Gonometa* virus.

It is not clear why the response involves only IgM antibodies but this could be explained on the basis of a low but frequently repeated stimulus. There are several reports in the literature of the presence of virus-neutralizing substances in the sera of animal species not regarded as natural hosts. Cattle sera from Sierra Leone, Ghana, Uganda, Sudan and Kenya contained neutralizing substances, probably antibodies, against yellow fever virus⁷. This was also true, however, of 3/40 cattle sera

from India and 1/153 from England and France, where exposure to infection with yellow fever virus could be ruled out. The phenomenon of neutralizing substances to polio virus in cows has been reviewed⁸; serum from 75–90% of cattle over three years of age neutralized not only type 2 polio virus but also type 1 and occasionally type 3. The neutralizing substances were usually present in low titre but possessed all the properties of antibody in human sera, including a predominant association with the gamma globulin fraction. In calves of four to six months of age, neutralizing substances were rarely found. A significant feature of this work was that calves without neutralizing antibody could not be infected with a virulent strain of polio virus, irrespective of portal of entry, and moreover failed to develop antibodies to it. Sabin⁸ concluded that "in cattle, at least, the antibody appearing in low titre with advancing age was probably the result of infection with another agent possessing antigenic groups that are related to those of poliomyelitis virus". A more recent observation is the presence in pigs in Japan of high levels of neutralizing antibody to *Nodamura* virus⁹, which has been tentatively classified as a picornavirus¹⁰. Neutralizing antibody was also found in 1/54 herons and egrets⁹, and it was concluded that pigs were the likely source of *Nodamura* virus, since they were frequently bitten by *Culex tritaeniorhynchus*, the mosquito from which the virus was first isolated. The nature of the neutralizing antibodies has not been determined, so it is not known if IgG or IgM is involved.

These observations with *Gonometa* and *Darna trima* viruses have implications relating to the control of insect pest populations by the deliberate release of viruses. While it is probably true that most insect viruses exhibit a high degree of host specificity and thus have great potential in biological control programmes, it is obviously desirable that sound experimental data should be available to check this specificity. It seems unlikely that the antibody to the two insect viruses resulted from infection and multiplication of similar agents in the mammalian hosts. The IgM response implies repeated low level exposure to the antigen concerned which must therefore be widely distributed in the environment. The close relationship of these antigens to the two viruses suggests the existence of viruses in some host population, possibly arthropod, in the areas from which our serum samples were drawn. The ubiquity of these agents and the apparent regularity with which they can reach mammalian hosts stress the risks which might arise from the deliberate release of virus to control insect pest populations, should the viruses used exhibit wider host specificity than expected.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Another Test of Space-Time Curvature and Relativity

Now* that Sir Arthur Eddington has successfully measured the space-time curvature by the edge of the Sun, thereby confirming Dr Einstein's remarkable forecast, an additional test of relativity comes to mind.

Obviously space must be curved through a physical fourth dimension. The fact that we cannot actually see the curvature should not cloud our perception of it. Minkowski by his interpretation of $\sqrt{-1}$ provides a precise mathematical demonstration of the curvature of space to form the hypersurface of a hypersphere. Therefore light coming to us from distant sources must necessarily have traced out this space-time curvature. In other words, it must have been on the average in a constant state of acceleration throughout the journey from its source.

When Heinrich Olber propounded his paradox in 1826 almost one hundred years ago, he assumed that the intrinsic brightness of starlight would remain unchanged, regardless of the distance traversed. He, of course, took it for granted that space was Newtonian space—"flat". With relativity this premise is altered. Space is curved through a fourth dimension; light following the curvature must be accelerating; and consequently the intrinsic brightness of starlight must be reduced to an apparent brightness in direct proportion on the average to the distance covered. Olber's paradox is thereby resolved.

Also, another test of relativity and space-time curvature is provided. By looking further and further out into space astronomers should be able to detect a red shift in starlight—a shift that increases in direct proportion to the distance covered. Perhaps when Dr Hubble gets his 100-inch telescope into operation the test will become feasible.

It is important, I believe, that astronomers should be informed now that the red shift is to be expected. Otherwise, when they find it, they may adopt a three-dimensional interpretation. If so, on the basis of a Doppler effect they could reach an erroneous conclusion that the universe was exploding. Nor can we count on the more conservative and orthodox physicists of today to correct the error. Being predominantly three-dimensional minded they might easily fall in with the same false reasoning. Such a calamity could set relativistic physics back by half a century.

In order to prevent this from happening it may be just as well to scotch such an interpretation at the outset. The correct interpretation is readily obtained by considering a three-dimensional analogy. Suppose a spherical balloon is covered with polka dots. From a two-dimensional viewpoint at the surface of the balloon light coming from distant polka dots would be coming around a curve. This three-dimensional curvature would be beyond the two-dimensional viewpoint. Yet the red shift in the light would be observable. It would be a shift that increased on the average in direct proportion to distance.

Now suppose the balloon was in the process of being blown

up to larger size. The polka dots would be spreading apart, thereby creating a Doppler-type red shift. At the same time, over a given distance, the rate of curvature into the third dimension would be decreasing, thereby decreasing the rate of acceleration and reducing the three-dimensional red shift. The two changes in the red shift would exactly offset each other, so that from the two-dimensional viewpoint at the surface of the balloon there would be no evidence that the balloon was expanding. The same in reverse would be true if the balloon was shrinking.

We in three-dimensional space which forms the hypersurface of a hypersphere are in a similar situation. There is no way we can observe whether our universe is expanding, contracting or stable. There is, of course, the question whether or not Dr Einstein's field equations provide for a stable universe. Yet that is a theoretical problem still moot. It would be unfortunate if the red shift, when it is discovered, should serve to obfuscate a solution to Dr Einstein's problem.

The important point is that by looking far enough out into space, astronomers should be able to detect a red shift in starlight. Moreover, this red shift when it is discovered will provide additional confirmation of Einsteinian space-time curvature and relativity.

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The Origin of the Moon

I HAVE some quantitative doubts concerning Anderson's proposals¹ that the Moon condensed from material off the median plane of the initial solar nebula.

First, the pressure range which he uses for his solar nebula seems to be rather high, and, of course, the partial pressures of the components will be well below the total. But a temperature adjustment could compensate for that. Much more serious is the fact that when condensation begins in the lower pressure region away from the median plane, the resulting dust particles will fall slowly through the residual gas towards this plane. The "scale height" for a dust particle with only 100 atoms in it will be 10 times less than that for one atom (in the absence of condensations the gravitational potential energy increases as the square of the distance from the median plane). Any heavier particles will necessarily and quickly congregate very close to the median plane, when they will be swept up by the developing Earth.

If the gas were dense, convective movements would no doubt modify extensively the distribution of both gas and dust, but would quite certainly not allow particles initially condensing off the median plane to remain there until they had formed the Moon.

If the bulk of the Moon is systematically more refractory than that of the Earth it seems to me inescapably to follow that it must originally have formed nearer the Sun.

All existing explanations of the Moon's origin are improbable—and perhaps need to be in view of the unique character of the Earth-Moon system—but if it had formed within the orbit of Mercury, a resonant interaction with the

* Copy of a manuscript found in the drawer of a desk built in 1922. Communicated by H. W. Grayson.

latter might have led to its ejection, leaving Mercury in a highly eccentric orbit which has even yet not become so nearly circular as the orbits of Venus or Earth².

Although I do not believe Anderson's theory of the formation of the Moon, his idea of differential volatility may be important.

To me, it seems easier to believe that the material of the planets was collected by the Sun in passing through a cold dust cloud rather than from the remains of the solar nebula. A dust cloud would have an angular momentum, resulting from its motion around the centre of the Galaxy, of the right order of magnitude for our planetary system—whatever redistribution between it and the Sun might later occur—and the evaporation of the more volatile particles as they approached the Sun from all sides would build up an adequate capture mechanism both for each other and for more refractory particles.

Whether or not this was so, if the actual accumulation into planets took place with the Sun close to its present temperature, it is important that water, surely the most abundant compound of oxygen and hence perhaps of all elements, would be in the form of dust further away from the Sun than the asteroids but in the form of gas within this region.

Clearly gases could not have contributed to the primary aggregation leading to the inner planets, which would have been within the Roche limit for any reasonable gas pressure.

It seems uneconomical to have a different mechanism for the accumulation of the outer planets, and the properties of water give us the opportunity to use the same mechanism and still explain their very different structure. The presence of ice crystals in quantity will have led to a discontinuous rise by a large factor in available material beyond the asteroid belt, leading to a faster and earlier beginning for the major planets. These would then have reached a mass which could capture first methane and then hydrogen well before the inner planets could do so and hence, as observed, have swept up almost the whole of the system's supply before the Earth and Venus were big enough to take their share.

I am not confidently supporting Ovenden's³ proposal for a planet 90 times the mass of the Earth in the region of the asteroids, because I do not see how one can be sure that small cumulative errors do not invalidate his calculations. Nevertheless, if this had been formed chiefly of water and hydrogen, and its destruction had been due to its orbit coming into resonance with Jupiter and its consequent deflexion to an approach within the Roche limit, there would be no problem of accounting for what had happened to 99.9% of its mass. Jupiter will have it, but a belt of gas might have persisted for long enough to bring the residual solid particles back to their present orbits.

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¹ Anderson, D. L., *Nature*, **239**, 263 (1972).

² Cameron, A. G. W., *Nature*, **240**, 299 (1972).

³ Ovenden, M. W., *Nature*, **239**, 508 (1972).

Bode's Law

M. W. OVENDEN¹ has outlined a theory intended to provide a dynamical explanation for Bode's Law. I suggest instead that the approximately constant spacing ratio expressed in Bode's mnemonic can be generated by a sequence of random numbers subject to the constraint that adjacent planets cannot be "too close to each other". The physical basis for the constraint is that if in the process of accretion two planets were "too close

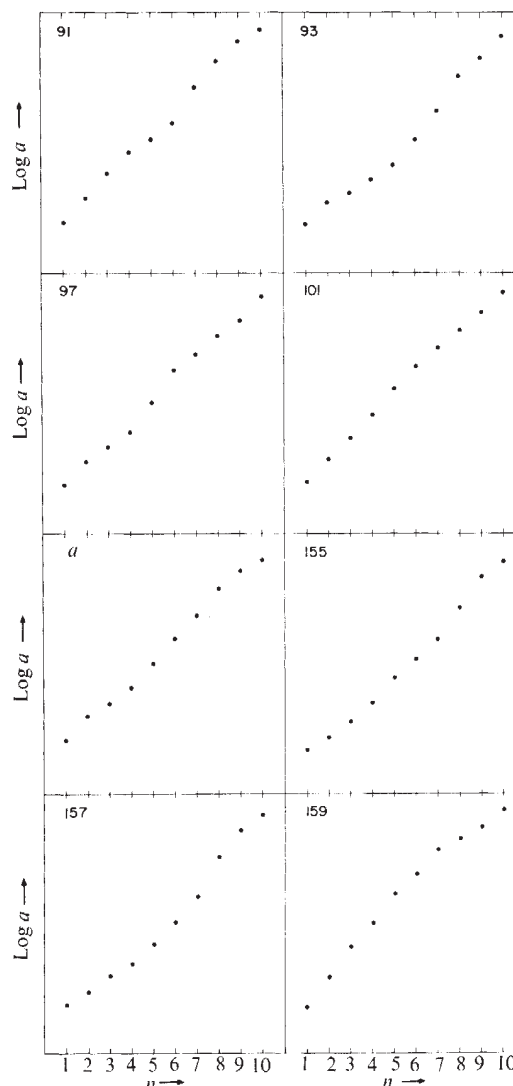


Fig. 1 Bode's Law for computer-simulated planetary systems.

to each other", they would coalesce or cease to grow because they were competing for the same material. Such a constraint was embodied in a series of computer-generated planetary systems published by S. H. Dole². Dole generated planets by injecting nuclei into a Laplace-type nebula and allowing them to accrete dust and also gas (if their mass was sufficiently large and their temperature sufficiently low). He kept track of the dust and gas accreted (so that it could not be used twice) and coalesced planets if their orbits crossed. The initial semimajor axes of the proto-planets were chosen at random.

In Fig. 1 is plotted the logarithm of the semimajor axes (a_n) against the planet number (n) for seven of Dole's computer-generated planetary systems and for the Solar System. The reader is invited to pick out the Solar System. (The label for the Solar System in binary is 111001. The remaining labels are Dole's.)

The slopes $(\log(a_9) - \log(a_2))/(9 - 2)$ cover a narrow range bracketed by the slopes of the lines in Fig. 2. The fractions to the right of each line give the ratio of adjacent planetary periods corresponding to the plotted ratio of semimajor axes. It is seen that within this narrow range the ratio of periods is always close to that of two "small" integers.

I conclude that this offers an equally satisfactory rationalization of Bode's mnemonic. Further, I suggest that the closer spacing of the satellite system compared with the spacing of planets in the Solar System might be accounted for by the fact that the satellites did not grow to a size where they accreted gas (in addition to dust) and that their accretion was not

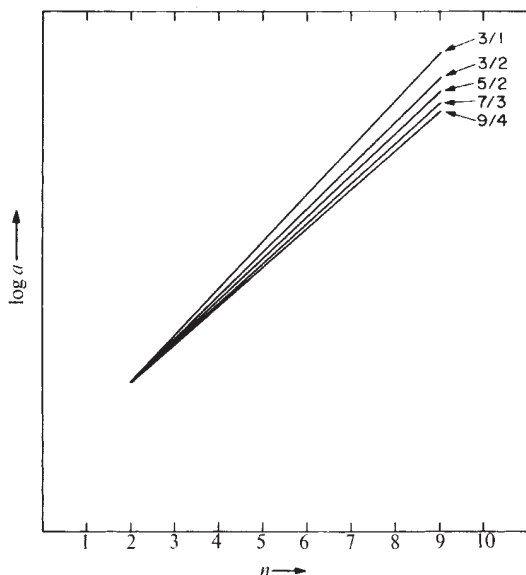


Fig. 2 Slopes for which ratio of adjacent periods is rational.

appreciably helped by their self-gravity. Thus they consumed a smaller fraction of their surrounding nebula and could be formed closer together. A computer simulation of satellite systems, following Dole's model, would provide evidence with which to evaluate this speculation.

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Underabundance of Ionized Helium in the Galactic Centre

GAMOW¹ suggested in a classical paper that the present element abundances (in particular the light elements H, D, He and Li) may have been formed during the first few minutes of the birth of the universe. This suggestion received further support after the 3 K background radiation, also implied in that paper and numerically predicted by Alpher and Herman², was

detected by Penzias and Wilson³. There are, however, still serious objections to a primordial origin for helium.

The most direct method of determining helium abundances in our Galaxy with the least number of complicating assumptions is the observation of hydrogen and helium radio recombination lines in HII regions. The basic method, its assumptions, and its uncertainties are discussed in, for example, refs. 4, 5. If we assume that hydrogen and helium are homogeneously mixed and that hydrogen is ionized wherever helium is ionized, then the total helium abundance is given by

$$\frac{N_{\text{He}}}{N_{\text{H}}} = \frac{N_{\text{He}}^0}{N_{\text{H}}^+} + \frac{N_{\text{He}}^+}{N_{\text{H}}^+} + \frac{N_{\text{He}}^{2+}}{N_{\text{H}}^+}$$

The second and third terms on the right can be determined by observation of radio recombination lines.

Most cosmological models predict a helium abundance of approximately 10% by number. In an effort to determine whether this value holds throughout our Galaxy we have observed hydrogen and helium radio recombination lines in 40 galactic HII regions. These data will be published in detail later (Churchwell, Mezger and Huchtmeier). A brief summary of the primary results is as follows:

There are HII regions, such as NGC 2024 and M43, with a very low $N_{\text{He}^+}/N_{\text{H}^+}$ ratio. These are HII regions whose exciting stars are of spectral type O9 or later. Theoretical considerations⁶ show that stars with such low effective temperatures cannot ionize a substantial amount of helium.

All HII regions located at galactic radii $R \gtrsim 3$ kpc which require for their ionization one (several) star(s) of spectral type O7 or earlier have abundances in the range

$$5\% \leq N_{\text{He}^+}/N_{\text{H}^+} \leq 12\%$$

with most values clustering around 9%. This result supports the conclusion drawn from an analysis of various observational methods that the He-abundance at least within our Galaxy is constant and has a value (number ratio) of about 10% (ref. 7).

In agreement with estimates of the effective temperatures of early-type stars, the amount of doubly ionized helium, He^{2+} , in galactic HII regions is negligible.

Only in the case of three giant HII regions (the definition of a giant HII region is that its intrinsic radio flux density for $\tau_c \ll 1$ is equal to or greater than four times the flux density of the Orion Nebula) with projected positions close to the galactic centre was it not possible to detect helium lines^{8,9}. We have investigated the distribution, distance and kinematics of the ionized hydrogen towards the galactic centre region, and conclude that giant HII regions located within $-1^\circ \leq l^{\text{II}} \leq +1^\circ$ and close to the galactic plane have actual distances of less than 150 pc from the dynamical centre of the galaxy¹⁰.

The possibility that the helium might be in the doubly ionized state prompted us to search for the $\text{He}^+173\alpha$ line in

Table 1 Observed Helium Abundances

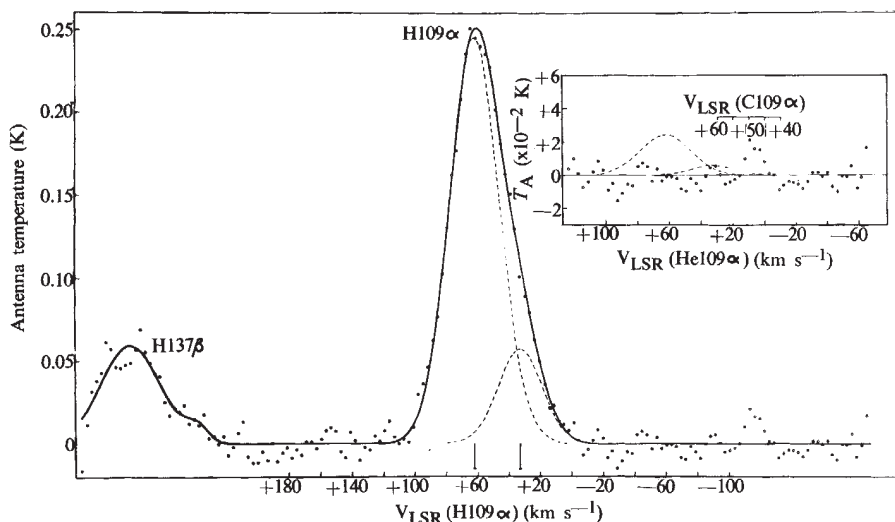
Source	HPBW (arc min)	Integ. time (min)	Transition	T_L (K)	$\frac{\epsilon(137\beta)}{\epsilon(109\alpha)}$	$\epsilon = \int T_L dv$ (K kHz)	$\frac{N(\text{He}^+)}{N(\text{H}^+)}$	$\frac{N(\text{He}^{2+})}{N(\text{H}^+)}$	Ref.
G0.2-0.0	6	510	H109 α	0.247 ± 0.006	—	200 ± 17	≤ 0.025	≤ 0.008	
	6	510	He109 α	≤ 0.006	—	≤ 5			
	6	666	He ⁺ 173 α	≤ 0.008	—	≤ 6			
G0.5-0.0	4	105	H109 α	—	—	—	≤ 0.041		11
	4	105	He109 α	—	—	—			
G0.7-0.0	6	450	H109 α	0.245 ± 0.005	0.257 ± 0.035	141 ± 16	≤ 0.021	≤ 0.005	
	6	450	He109 α	≤ 0.005		≤ 3			
	6	494	He ⁺ 173 α	≤ 0.005		≤ 3			
	4	75	H109 α	—		—			
	4	75	He109 α	—		—	≤ 0.039		11

For sources G0.2-0.0 and G0.7-0.0 only data for the main line components are reported.

To obtain $N(\text{He}^+)/N(\text{H}^+)$ we assumed that $\Delta v_L(\text{He}) = \Delta v_L(\text{H})$ where Δv_L is the line width at the half-intensity point.

Neither T_L nor ϵ values are given by ref. 11.

Fig. 1 109 α recombination spectrum of G0.7-0.0. —, Best fit to the observed data points; ---, the two gaussian components of the H109 α line, determined by a best fit decomposition. Inset: the expected He109 α profile which was obtained by scaling the H109 α profile by a factor of 0.1 and shifting it by +2.041 MHz with respect to the centre frequencies of the two H109 α components. A C109 α line may be present with a velocity of $\sim +50$ km s $^{-1}$ to the high frequency side of where the helium lines are expected.



G0.7-0.0 and G0.2-0.0, with negative results. Recently, Huchtmeier and Batchelor, using the Parkes 210-foot telescope, have found an upper limit on the He $^{+}$ abundance in G0.5-0.0 considerably lower than the values given in Table 1.

Our observational results, obtained with the NRAO 140-foot telescope in conjunction with a 384 channel auto-correlation spectrometer, are compiled in Table 1. Also included are some earlier measurements¹¹ with the Parkes 210-foot telescope.

G0.5-0.0 has a gaussian hydrogen line shape, whereas G0.2-0.0 and G0.7-0.0 have more complex hydrogen line shapes which can be interpreted as a superposition of several velocity components. Fig. 1 shows as an example the 109 α recombination spectrum of G0.7-0.0.

The two gaussian components (best-fit) are indicated by dashed curves. The inset in Fig. 1 shows the expected He109 α profile.

The abundance of He $^{+}$ in all these HII regions is less than 2%. (We include G0.5-0.0 on the basis of the Huchtmeier and Batchelor results.) The abundance of He $^{2+}$ in G0.2-0.0 and G0.7-0.0 is less than 1%. Either the helium is essentially all neutral or there is no helium in the galactic centre. We will briefly discuss these two possibilities.

It has been shown that these nebulae are similar to giant spiral arm HII regions such as W49A (ref. 10). The number of 09-stars that would be required to ionize these HII regions makes ionization by such cool stars unlikely, unless the luminosity function of 0-stars in the centre region is drastically different from that in the solar vicinity. This, together with the results of Rubin⁶, makes it rather unlikely that a large fraction of helium in these HII regions exists in the neutral state. This would imply that there is an actual underabundance of helium in the galactic centre.

The cosmological implication of a helium underabundance in the galactic centre would be far reaching. We do not overlook that there are also a number of giant spiral arm HII regions with an abundance of He $^{+}$ considerably less than 10%. On the other hand, in no giant spiral arm HII region do we observe an abundance of He $^{+}$ as low as 2%. Our observations of the galactic centre region, however, show that $N(\text{He}^{+})/N(\text{H}^{+})$ and $N(\text{He}^{2+})/N(\text{H}^{+})$ are respectively $<2\%$ and $<1\%$. Therefore, 70% of the total helium content in the galactic centre HII regions would have to be neutral if the He abundance were the same as in the spiral arms. The NRAO is operated by Associated Universities, Inc., under contract with the National Science Foundation.

Table 2 Characteristics of HII Regions

Source	Size θ_{α} (pc)	θ_{δ} (pc)	D kpc	$S_{5 \text{ GHz}}$ f.u.	L_c s $^{-1}$	No. of stars required	
						07	09
G0.2-0.0	51	15	10	157	1.65×10^{51}	97	424
G0.5-0.0	13	16	10	35.5	3.04×10^{50}	18	78
G0.7-0.0	9	11	10	47.8	4.63×10^{50}	27	119

Some characteristics of the HII regions, derived from continuum observations at radio wavelengths, are compiled in Table 2. The data for the source size (columns 2 and 3) and flux density at 5 GHz (column 5) were taken from Reifenstein *et al.*¹². The Lyman continuum photon flux required to produce the measured radio flux density (column 6) was derived using the relation (valid for $\tau_c \ll 1$)

$$\left[\frac{L_c}{\text{s}^{-1}} \right] = 4.76 \times 10^{48} \left[\frac{\nu}{\text{GHz}} \right]^{0.1} \left[\frac{T_e}{\text{K}} \right]^{-0.45} \left[\frac{S_{\nu}}{\text{f.u.}} \right] \left[\frac{D}{\text{kpc}} \right]^2$$

where $\nu = 5$ GHz was assumed, the flux density ($S_{5 \text{ GHz}}$) was taken from column 5, and the electron temperature (T_e) and distance (D) were assumed to be respectively 8,000 K and 10 kpc. Using the L_c values as a function of spectral type¹³ the numbers of 07 and 09 main sequence stars required to ionize these nebulae are given in columns 7 and 8 respectively.

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Infrared Photography of OH Airglow Structures

INFRARED airglow emission is bright, patchy and erratic^{1,2}. The primary source of this emission was identified by Meinel³ as rotation-vibration bands of the OH molecule. These and subsequent studies⁴⁻⁶ did not delineate the true morphology of the infrared night sky because large fields of view (~ 20 deg²) were used and only point by point measurements taken. Accurate mapping of the night sky requires a small field of view to resolve the smallest structures and a rapid scanning rate to "freeze" any time variations in the luminosity.

We have carried out a study at $2.2\ \mu\text{m}$ (ref. 7), using an infrared photometer with a 1.4 square degree field of view scanning at $12\ \text{deg min}^{-1}$, and a similar study at $1.65\ \mu\text{m}$ (ref. 8) with a 0.7 square degree field of view. At both wavelengths many small bright patches were resolved which had lifetimes of tens of minutes. During these studies, we decided to attempt to photograph the night sky with the relatively new Eastman Kodak High Speed Infrared film and a fast 35-mm camera. An $f/1.2$ lens was used with a Wratten 88A filter to isolate the spectral region from $7400\ \text{\AA}$ to the emulsion cutoff at $9000\ \text{\AA}$.



Fig. 1 A 15-min exposure of the eastern sky on December 1, 1972, at Capilla Peak Observatory (2,855 m). The maximum in brightness below the centre of the frame, in spite of vignetting, is characteristic of the airglow distribution. A tree top appears above the depressed horizon.

Surprising results were obtained from a series of 60 consecutive 15-min photographs, taken during the moonless portions of the nights of December 1 and 2 at Capilla Peak Observatory (altitude 2,855 m). During this period the sky was continuously cloud-free, high flying aircraft left no enduring condensation trails, and no aureole was visible near the Sun. The photographs all show bright cloud-like structures which moved on the sky and varied in brightness. In these and about 80 subsequent photographs (taken 15 km west of Albuquerque, altitude 1,800 m) the predominant features observed in the eastern and western sky are elongated bright bands inclined somewhat to the horizon (Fig. 1). A large band moving towards the southwest horizon on December 22 is shown in Figs. 2 and 3. The patches in the southern sky seem to be more rounded and mottled (Fig. 4) than when viewed to the east or west. Before and during the exposure of Fig. 4, our $1.65\ \mu\text{m}$ scanning photometer recorded an extremely bright spot in the direction of the centre of this frame. The features of Fig. 4 resemble an auroral corona, an impression exaggerated by the vignetting seen in all the photographs.

Could these cloud-like features indeed be merely clouds? We do not accept such an identification because no clouds could be detected visually anywhere in the sky during twilight or after



Fig. 2 A 10-min exposure of the southwest sky on December 22, 1972, from 15 km west of Albuquerque (1,800 m).

moonrise during these observing periods; all photographs show the sky brightness increasing toward the horizon as is expected for an emitting layer in the upper atmosphere (the Van Rhijn effect, well known to airglow observers); simultaneous photographs of the same area were taken on nights when there were clouds, with both panchromatic and infrared film. The trails of stars were modulated by the clouds and occasionally interrupted completely. No strong modulation of the star trails is present when stars pass through either the bright or dark bands which are photographed on clear nights. There is, however, a slight modulation of the star trails caused by pre-exposure, over-exposure, and vignetting effects. We conclude that these structures are indeed due to varying airglow emission and not to any type of modulation of a uniform background by atmospheric clouds, dust, or haze.

In addition to the inherent interest of being able to photograph with high angular resolution the complex airglow structures present in the infrared sky, such photographs will provide other information.

Motions of bright patches in the upper atmosphere, whether due to winds, gravity waves, or some process related to the Earth's magnetic field, are readily deduced. Assuming a height of 100 km, in accordance with the most recent direct rocket measurements^{9,10}, the southward component of velocity of the wide bright band near the top of Figs. 2 and 3 is about $20\ \text{m s}^{-1}$. On December 23, a small, bright feature in the western sky was moving due south at $43\ \text{m s}^{-1}$. Thus,



Fig. 3 A 10-min exposure of the same area as in Fig. 2, 30 min later. Note the motion of the broad band above the bright star trail (Fomalhaut) in the upper right. The bright stripe in the centre of the frame has elongated and moved to the right. Other variations in brightness and position of patches are apparent.



Fig. 4 A 15-min exposure on the southwestern sky from Capilla Peak on December 1, 1972. Photographs of this area were taken when an enhancement was recorded by our $1.65 \mu\text{m}$ scanning photometer. Mottled structures seem to be characteristic of the southern sky. The observatory dome and a tree top appear at the bottom of the frame.

synoptic maps of upper atmospheric "wind" speeds at the OH layer can be determined on a world-wide basis rather than relying on vapour releases from rockets or the analysis of enduring meteor trails.

Also, observations of a bright spot from two widely separated sites will yield parallax determinations of the height of the OH emitting layer; we need no longer rely on infrequent rocket measurements at a few places. Parallax measurements on different sized emission patches may yield information on the distribution of the patchiness with height and the frequency function of turbulent cell sizes.

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Fission Track Dating of the Obsidian of Lipari Island (Italy)

Obsidian was widely traded in prehistoric times, and it is of particular interest to archaeologists to reconstruct the trading patterns¹⁻⁵. One possible source of obsidian for prehistoric man is Lipari Island (Eolie Archipelago, Italy) and we have dated obsidian flows there for two chief reasons: first, to find out which of these flows could have been used by primitive man, and second, because we wished to identify the artefacts

that have been found at various sites in the Mediterranean basin.

There are three principal obsidian flows on the island of Lipari. Two of them (Forgia Vecchia and Rocche Rosse) were produced by eruptions which took place during historic times. In fact Keller⁶ used the radiocarbon method for dating a palaeosoil stratigraphically below the Forgia Vecchia flow, and obtained dates ranging from 4,800 to 1,220 BP. All those who have studied the Rocche Rosse flow assign it to the volcanic event that has been dated at AD 500-550.



Fig. 1 Location of the archaeological sites investigated. 1, Monte Aquilone; 2, Catignano; 3, Fossa Cesia; 4, Lipari; 5, Filicudi.

The Acquacalda pumices enclose some obsidian pebbles. These pumices were produced in the same eruptive event, but the pebbles predate them (we have already published an age of $21,000 \pm 4,000$ years for them). Apart from these pebbles, only the Gabelotto obsidian flow may be archaeologically interesting, because of its age. Keller⁷ dates it as 4,800 to 12,920 BP. These age measurements have been obtained by the ^{14}C method on sites that can be correlated stratigraphically with the flow itself.

Table 1 Dating of Lipari Obsidians

Flow	ρ_F	Φ	ρ_I	Age (yr)
Rocche Rosse	3.2	0.72×10^{15}	102,000	$1,400 \pm 450^*$
Forgia Vecchia	4.2	0.99×10^{15}	160,000	$1,600 \pm 380^*$
Gabelotto	26.7	0.72×10^{15}	104,000	$11,400 \pm 1,800^*$

ρ_F = fossil tracks/cm²; ρ_I = induced tracks/cm².

* The experimental errors include both the counting error and the uncertainty in determination of the thermic neutron dose.

The values obtained for Lipari obsidians are listed in Table 1. The high experimental error associated with the youngest samples is a consequence of the small number of fossil tracks counted. On the other hand, we thought it inappropriate to lengthen the scanning time, for these values, like those reported in the literature, mean that flows could not have been used as a source of obsidian in prehistoric times. Our results confirm the assignation of the two obsidians to the same recent event. We wish to emphasize the excellent

agreement of our results with those radiocarbon ages reported by Pickler⁸ and Keller^{6,7}.

The source of the obsidian artefacts can be identified in several ways—for example, by studying the chemical and physical properties of the material itself⁹. We have tried to solve the problem by comparing the age of the material of the archaeological samples with that obtained for geological samples collected from the probable obsidian sources.

We have examined artefacts found on the islands of Lipari and Filicudi in order to find out which material was used in prehistoric times. The study has also been extended to artefacts from sites on the Italian Adriatic slope. The results are shown in Table 2.

Table 2 Dating of Artefacts from the Italian Archaeological Sites

Site	Sample	ρ_F	Φ	ρ_I	Age (yr)
Monte Aquilone (Manfredonia)	1	37	0.80×10^{15}	166,000	$11,000 \pm 2,900$
	3	27	0.80×10^{15}	168,000	$8,000 \pm 3,500$
	4	30	0.80×10^{15}	118,000	$12,500 \pm 5,000$
Catignano (Chieti)	CH 1-1	30	0.80×10^{15}	152,000	$10,000 \pm 3,000$
	CH 1-2	—	0.80×10^{15}	155,000	—
	F 1-2	31	0.80×10^{15}	138,000	$11,000 \pm 2,700$
Fossa Cesia (Pescara)	FR 2	24	0.80×10^{15}	123,000	$9,700 \pm 3,000$
	F 261	30	0.80×10^{15}	125,000	$11,900 \pm 2,200$
	F 2-2	36	0.80×10^{15}	150,000	$11,800 \pm 3,400$
Lipari scavo	1	27	0.67×10^{15}	106,000	$10,500 \pm 2,800$
Filicudi	1	31	0.67×10^{15}	128,000	$10,100 \pm 2,500$
	3	32	0.67×10^{15}	119,000	$11,200 \pm 3,000$

Comparing Table 1 with Table 2 we conclude that: (1) the Gabellotto obsidian was the only one used in prehistoric times on Lipari Island; this material was evidently transported by prehistoric man to the Adriatic shore of Italy; (2) the fact that the same age was obtained for samples both from the flows and from far away from the island means that the volcanic events that occurred after the artefacts left Lipari did not produce fading of tracks in Gabellotto obsidian; we have also shown this by measuring the sizes of fossil and induced tracks that have undergone the same chemical etching¹²; (3) as the identification of artefacts by the fission track method is very rapid, we believe that the study should be extended considerably to all the Mediterranean basin sites, in order to mark the geographical and chronological boundaries of obsidians that have affected the basin itself.

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Bioturbation of Superficial Marine Sediments by Interstitial Meiobenthos

IN a recently completed series of laboratory studies, lebensspuren were produced by individual macrobenthic organisms on a variety of marine sand and mud substrates (freshly collected from depths down to 30 m in the Bristol Channel), from which all other macrofauna had been removed by passing it through a 1.0 mm mesh. But the resultant tracks, trails and burrows gradually disappeared when the aquarium tanks containing them were left undisturbed after the termination of the experiments.

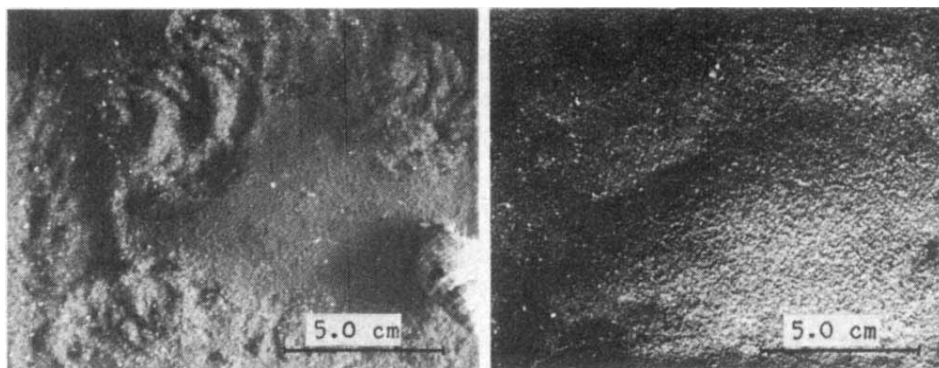
This effect was investigated by controlled experiments, in which macroorganisms and aerators were removed from the aquaria immediately after lebensspuren formation, and great care was taken to eliminate all extraneous vibrations. Progressive blurring of tracks and trails on both sand and mud surfaces became apparent after about 48 h, and, by the end of 10–14 day, all but the deepest marks had been obliterated (Fig. 1). Clearly, the erasure of lebensspuren was caused by small scale biogenic activity within the sediments themselves, and stereomicroscopic examination through the transparent aquaria walls invariably disclosed a copious interstitial meiofauna in the surface sediment layers.

Ostracods and nematodes were the most widely distributed and active members of the meiofaunas, but copepods, malacostracans, archiannelids and juvenile molluscs were locally abundant. The movement of sediment particles by ostracods, as viewed through the microscope, was particularly spectacular. Averaging about 0.5 mm in length, these free-ranging crustaceans were seen burrowing down at least 4.0 mm into the sediment, jostling aside sediment grains several times their own size with a vigorous, jerky motion, and disrupting the sediment fabric within their immediate vicinity. Such activity, continued over a prolonged period by a sufficiently dense population, obliterated biogenic and purely inorganic structures at and near the sediment surface. Meiobenthic copepods and malacostracans exhibited similar behaviour, but their capacities for burrowing and movement of sediment particles varied according to their size and vigour.

The activity of interstitial nematodes was different. These organisms rapidly established an intricate, closely spaced network of thread-like intergranular burrows within the surface layer of freshly emplaced sediment (Fig. 2), through which they could be observed gliding at relatively high speeds, estimated at 2–3 mm s⁻¹. The nematode burrows often persisted for several hours until obliterated by the activity of other organisms, their persistence presumably indicating reinforcement by mucus secretions. Attempts to confirm such a specific function for the abundant mucus present in the sediments by staining with thianin and mucicarmine were, however, unsuccessful. The formation of such a reticulate burrow system would undoubtedly promote downward percolation from the overlying waters into the surface sediment layer. Thus, bioturbation by interstitial nematodes and associated meiobenthos was an important factor influencing the development of a pale brown, oxidized, surface layer, 0.5–1.5 cm thick, which was observed forming within a few hours of emplacing black, anoxic muds in the aquaria. Comparable brown to reddish layers are repeatedly noted in the Challenger Expedition report¹ on deep sea deposits, and, as surfacing core and grab samples from sheltered environments on the New Zealand continental shelf and slope down to depths of at least 2,000 m, in unpublished records of the New Zealand Oceanographic Institute.

The meiofaunas observed in the laboratory all originated in shallow water deposits of the Bristol Channel. Interstitial meiofaunas are generally abundant^{2–6} in littoral, inter-tidal and shallow near-shore regions; but in such high energy environments their sedimentological effects are masked by wave and current action and macrobenthic bioturbation. Nevertheless, small scale meiobenthic bioturbation, although frequently

Fig. 1 (Left) Lebensspuren made by the hermit crab, *Eupagurus*, on a surface of medium to fine sand. The broad, lunate markings were made during microphagic feeding; the lower, feathery track results from normal locomotion. (Right) The same surface after being protected from external disturbance for 12 days. Only the deepest gouged markings remain.



ignored, is simultaneously in progress and microenvironmentally extremely significant. Sheltered enclaves undoubtedly exist on continental shelves (for example, enclosed inlets on ria coasts and local tectonic depressions), where hydrodynamic conditions and bottom configuration are so subdued that meiobenthic bioturbation becomes a locally prominent sedimentological process.

Quantitative analyses of samples from off the east coast of the United States indicate⁷ consistent numerical ratios of macro- to meiobenthos of 1:70, and wet weight ratios per unit volume of sediment of 24:1. Because the latter figure embodies no correction for factors such as molluscan shell and foraminiferal tests, it may not provide a reliable measure of the relative bioturbation potentials of the two categories of benthic organisms. But meiobenthos has a much wider dissemination than macrobenthos within the sediments, so the nature of meiobenthic bioturbation, although less obvious, is much more diffuse.

A correlation between bottom sediment composition and meiofauna distribution is frequently indicated⁷⁻⁹, the larger populations usually inhabiting the coarser, sand-grade sediments. In the case of ostracods, however, Puri⁹ has found that the converse applies, and he states that "the population of ostracods increases seawards with the decrease in grain-size of particles" and that "the largest populations are confined to fine-grained clastics like clays and fine silts". This disclosure is of special interest in demonstrating that the finer grained sediments, with limited intergranular pore spaces, are not invariably impoverished in meiofauna.

Wigley and McIntyre⁷ noted an overall decrease in meiobenthos populations with increasing depth, although their sampling was restricted to regions shallower than 600 m. More recently, Tietjen⁸ and Coull¹⁰ have extended quantitative analyses of deep sea meiobenthos to depths exceeding 2,000 m off the east coast of the United States, Tietjen's data confirming appreciable decreases in overall numbers of meiobenthic organisms, and the complete disappearance of some meiofaunal groups, in sediments of the deeper seafloor. These findings are not entirely consistent with Thiel's¹¹ work on deep sea samples collected off the East African coast, in which he establishes the

presence of larger meiobenthos populations at depths around 4,000–5,000 m than at 1,000 m. Further quantitative information is clearly required concerning abyssal meiobenthos, but, even if deep sea meiobenthic communities are much sparser than their counterparts in shallower waters, their bioturbational effects, in a low energy environment with low rates of accumulation, may well assume a far greater significance. Thus, even on the deep seafloor, macrobenthic lebensspuren may have to be regarded as essentially short-lived phenomena, surviving more than a few days only if conditions at the sediment surface are sufficiently abnormal to inhibit the presence of meiobenthos. It follows that meiobenthic bioturbation is a factor to be considered, in addition to the better known physical and biological marine processes, when relating lebensspuren distributions to macrobenthic population densities, either on the modern seafloor or in ancient sediments.

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Fig. 2 Intricate network of closely spaced nematode burrows in sandy mud, viewed through glass side wall of aquarium tank.

Observations on Lake Sediments using Fallout ¹³⁷Cs as a Tracer

SIGNIFICANT levels of caesium-137 from tests of nuclear weapons were first detected in the atmosphere in 1954; the maximum deposition¹ occurred in 1963. It would be expected that a continuously accumulating lake sediment would incorporate ¹³⁷Cs from fallout in a distribution pattern similar to that found from regular analysis of rain and air-borne particulate matter, provided that there has been no significant

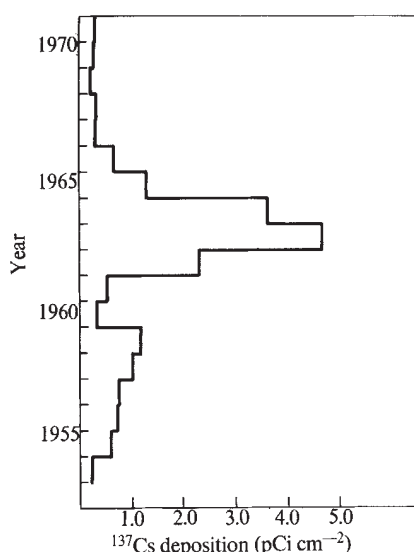


Fig. 1 Estimated annual deposition of ^{137}Cs at Windermere.

mixing in the sediment by diffusion or by the bottom fauna. Sediments from five lakes of the English Lake District have been analysed for ^{137}Cs in order to test this hypothesis (Table 1).

Table 1 Sizes and Natures of Five Lakes Studied

	Length (km)	Area (km ²)	Maximum depth (m)	Productivity	
				Trophic status	Minimum dissolved oxygen %
Esthwaite Water	1.8	1.0	15.5	Eutrophic	0
Blelham Tarn	0.7	0.11	15.1	Eutrophic	0
Windermere	17.0	14.79		Mesotrophic	
North Basin			64		56
South Basin			42		25
Ennerdale Water	3.8	2.91	42	Oligotrophic	75
Wastwater	4.8	2.91	76	Oligotrophic	80

Cores were taken from the deepest part of each lake with a 1 m Mackereth corer², diameter 5.3 cm. Three replicate cores were extruded into 0.5 cm or 1.0 cm slices and combined. Samples were dried and analysed for ^{137}Cs by gamma ray spectrometry³ using germanium (lithium) detectors. Generally each aggregate sample was counted overnight to achieve the necessary sensitivity and the lower limit of detection was then equivalent to less than 0.1 pCi cm⁻² of sediment.

Fig. 1 shows the estimated annual deposition of ^{137}Cs by rain at Windermere, based on results for Milford Haven¹ adjusted for differences in rainfall and corrected for radioactive decay (half-life 30 yr) to the year 1971. Fig. 2 shows the distribution pattern of ^{137}Cs in the topmost 25 cm of sediment in Windermere (South Basin) and four other lakes. In Table 2 the balance of deposition between the lakes and catchment

areas is calculated. The resemblance between Figs. 1 and 2 indicates that ^{137}Cs is present in accordance with recorded annual variations in supply from rain since 1954, rather than with the cumulative deposit on the watershed. The longest profile, from Esthwaite Water, shows such good agreement with Fig. 1 that we regard this as strong evidence for the absence of significant vertical movement of ^{137}Cs after it reached the mud surface. The form of the Esthwaite distribution pattern seems to exclude either diffusion in interstitial water⁴ or mixing of sediment by the bottom fauna⁵ or from resuspension and redeposition of shallow-water sediment by wind-induced turbulence⁶⁻⁸. Because mixing processes would be expected to have maximum effect in the shallow and productive Esthwaite Water⁹ the close resemblance of the pattern of ^{137}Cs distribution in the Esthwaite sediments to the observed pattern of annual variation since 1954 argues against the existence of significant vertical mixing in any of these lakes, and for direct deposition by rain rather than erosion from the watershed. The elongated "tail" of the ^{137}Cs curve in the two shallow lakes suggests that small amounts of ^{137}Cs may have been carried down either by diffusion or the bottom fauna.

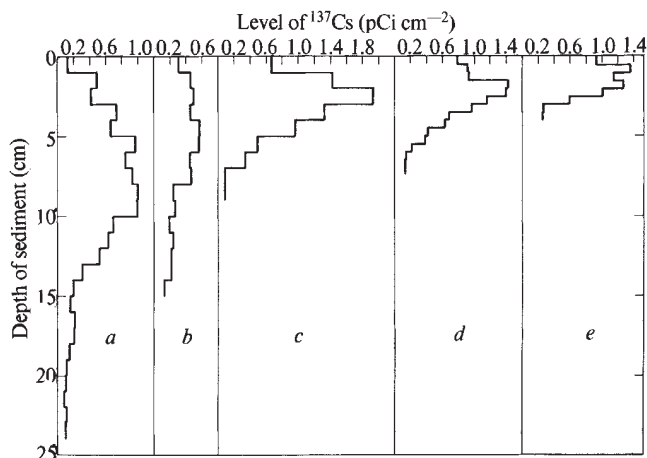


Fig. 2 Distribution of ^{137}Cs from fallout in the sediments of five lakes. a, Esthwaite Water, 1972; b, Blelham Tarn, 1970; c, Windermere, 1970; d, Ennerdale Water, 1971; e, Wastwater, 1971.

It therefore seems reasonable to accept that the position of the two horizons, the maximum deposition of ^{137}Cs in 1963 and the less precise first appearance in about 1954, indicate the depth of sediment accumulated in each lake since those dates. Table 3 shows the significantly higher accumulation rates since 1954 in the two shallow productive lakes, Esthwaite Water and Blelham Tarn, than in the deeper and less productive Windermere, Ennerdale Water and Wastwater. From work on the full sequence of postglacial sediments in these lakes¹⁰⁻¹² it is known, however, that the total depth of postglacial

Table 2 ^{137}Cs in Sediment and Catchment

	Total ¹³⁷ Cs in sediment (pCi cm ⁻²)	Total estimated surface deposition of ¹³⁷ Cs by rain (pCi cm ⁻²)	¹³⁷ Cs in sediment (pCi cm ⁻²)	Lake area	¹³⁷ Cs in sediment (pCi cm ⁻²)
			¹³⁷ Cs surface deposition (pCi cm ⁻²)	Catchment area	¹³⁷ Cs on catchment (pCi cm ⁻²)
Esthwaite Water	10.7	18.5	0.58	0.059	0.035
Blelham Tarn	5.2	18.1	0.29	0.036	0.010
Windermere	7.1	16.1	0.44	0.064	0.028
Ennerdale Water	10.1	24.4	0.41	0.066	0.027
Wastwater	6.2	26.0	0.24	0.060	0.014

The estimated surface deposition by rain (column 2) has been derived from the cumulative deposition at Milford Haven¹, adjusted in proportion to the rainfall for the individual lakes as estimated from the published figures for the nearest rain gauge²¹.

sediment, and hence mean annual accumulation rates over the past 10,000 yr, are much lower than these estimates based on ^{137}Cs distribution and show no correlation with these apparent differences between lakes with respect to accumulation rates since 1954 (see Table 3). The currently higher accumulation rates suggested by ^{137}Cs distribution for the two shallow productive lakes must therefore be of comparatively recent origin. Changes in populations of diatoms and invertebrates suggestive of recent eutrophication have been found in the topmost metre of sediment in Esthwaite Water^{13,14} and Blelham Tarn¹⁵⁻¹⁷. Smaller changes were found in the topmost 25 cm of Windermere sediment¹⁸ and Mackereth¹⁹ commented on the increase in sediment accumulation rate in this lake during the past 150 yr. The question arises as to whether cultural enrichment of a lake is accompanied by acceleration of the rate of accumulation of its sediments.

Table 3 Accumulation Rates, Present and Past

	On ^{137}Cs evidence From peak in 1963 (cm yr ⁻¹)	From tail in 1954 (cm yr ⁻¹)	On palaeo- magnetic evidence from about AD 1820 (cm yr ⁻¹)	Mean over past 10,000 yr (full postglacial profile) (cm yr ⁻¹)
Esthwaite Water	0.56-1.1	0.80-0.90		0.048
Blelham Tarn	0.57-0.71	0.90-1.0		0.045
Windermere				
North Basin				0.052
South Basin	0.29-0.43	0.45-0.50	0.2	0.032
Ennerdale Water	0.19-0.25	0.40-0.45		0.058
Wastwater	0.06-0.25	0.25		0.030

The overall similarity in total depth and type of postglacial sediments in all Lake District lakes has hitherto been accepted as evidence in support of Mackereth's²⁰ hypothesis that, until recently, most of the organic fraction of the sediment has been derived from the drainage basin and has therefore been qualitatively and quantitatively independent of lake productivity. The much higher rates of sediment accumulation since 1954 now suggested for the two eutrophic lakes by ^{137}Cs distribution indicate the possibility that post-eutrophication sediment may differ qualitatively as well as quantitatively from older sediments.

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Crystal Structure Elucidation by the Crystal Data Centre

KNOWLEDGE of the preferred conformation of chemical groups has been shown to be essential for the determination of the structures of biological molecules. The prime example is the elucidation of the structure of the α -helix for protein molecules by Pauling, Corey and Branson¹ from knowledge that the peptide group is coplanar and the importance of the hydrogen bond, whereas others had proposed incorrect structures owing to lack of this knowledge. On a more complicated scale, because the energy stabilizing the preferred conformation is less, but on an important biological scale, it was pointed out by Canepa, Pauling and Sörum² that the $\text{N}^+-\text{C}-\text{C}-\text{O}-$ group is synclinal. This was shown more clearly by Sundaralingam³ and recently shown to be true in solution by Partington, Feeney and Burgen⁴. The conformation of this group is of great importance in nervous transmitter substances⁵ and in phospholipids.

Esters are very common in biological substances and in drugs and, though it has been pointed out that esters are coplanar⁶, this result has been questioned by one theoretical calculation by Kier⁶ though confirmed by another theoretical calculation by Pullman *et al.*⁷. A less important example is the prediction of the structures of lysergic acid diethylamide and the hallucinogenic tryptamines and amphetamines⁸ on the basis of observed crystal structure analyses of the chemical subgroups, which have been confirmed by observation⁹.

The main method at present available for determining preferred conformations of organic chemical functional groups is that of statistical observation of known crystal structures. This is the reliable method used by all successful proposals of the structures of biological and chemical substances.

We have now developed a computer system for the systematic search of all known organic structures published since 1960 for chemical substructure and the calculation of the conformational parameters of the substructure. The first program of the system searches the merged Crystal Bibliographic and Data File prepared by the Crystal Data Centre in Cambridge, which was proposed by the late Professor J. D. Bernal, using an atom by atom search method for the particular group required. This program generates card images as input to our molecular geometry program (M. Dellow and P. P., in preparation) which calculates specified structural parameters of the desired group such as interatomic distances and angles, torsion angles and equations of planes with distances from the mean plane.

We have tested the system on a subset of the complete Crystal Bibliographic and Data File provided by the Crystal Data Centre in Cambridge. The subset contains 483 entries and has been searched for esters and for $\text{X}-\text{C}-\text{C}-\text{Y}$ groups. One hundred and sixty esters were found and it can be seen clearly from these results that in all observed cases the five atoms of the ester group are coplanar. Other more extensive rules for the preferred conformations of various types of ester are also indicated. The usually observed conformation of the $\text{N}^+-\text{C}-\text{C}-\text{O}$ groups is synclinal, though this group is sometimes observed as antiplanar in crystals⁵.

The systems are implemented on an IBM 360-65/I computer. The average atom by atom search time per table entry for esters was 1.315 s and the average molecular parameter calculation

time for each ester found was 4.380 s for interatomic distances and angles, torsion angles and the equation of the plane.

Having tested the system for specific groups on a subset of the Bibliographic and Data File, we can now make searches of the complete file for the determination of the preferred conformations of many organic chemical subgroups leading to stereochemical rules allowing the reliable prediction of the conformations of many biologically important molecules and drugs.

We thank Drs Olga Kennard, David G. Watson and William G. Town of the Crystal Data Centre for the provision of a subset of the Crystal Bibliographic and Data Files and for their help and assistance, and the Office for Scientific and Technical Information. The Crystal Data Centre is supported by the Office for Scientific and Technical Information (DES). This work is supported by the Medical Research Council and the Science Research Council.

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BIOLOGICAL SCIENCES

RNA in Coliphage T5

VIRUSES are thought to have either RNA or DNA as their genetic material, but not both¹, although oncogenic RNA viruses containing reverse transcriptase have been shown to contain some DNA. I did not expect to find that coliphage T5, a DNA-containing virus, also contained some RNA.

The bacterial strain (*Escherichia coli* F), the origin of coliphage T5⁺, and the media and conditions for their propagation have been described, as has the method of viable bacteria count, infectious titre and metabolic techniques². ³H-Leucine, ³H-thymidine and ³H-5-uridine were obtained from Schwarz BioResearch Inc. and ¹⁴C-thymidine from New England Nuclear Corp. Several preparations of ³H-5-uridine were used. The purity of each preparation was ascertained by paper chromatography in three solvent systems.

Infectious T5 bands at a density of 1.54 g cm⁻³ in a caesium chloride gradient (Fig. 1, and refs. 2 and 3). When bacteria were infected in the presence of ³H-thymidine or ³H-leucine the radioactivity was also recovered in the same density region (Fig. 1). This was expected as bacteriophage T5 is composed of DNA and proteins. When cells were infected in the presence of ³H-5-uridine, radioactivity was also incorporated into material banded in the same region as T5, and was not reduced by treatment with RNAase (Fig. 1). Electron microscopic examination of the material in the band (negative staining) revealed a preparation of uncontaminated coliphage T5. Rebanding of the ³H-5-uridine-labelled virus in a second

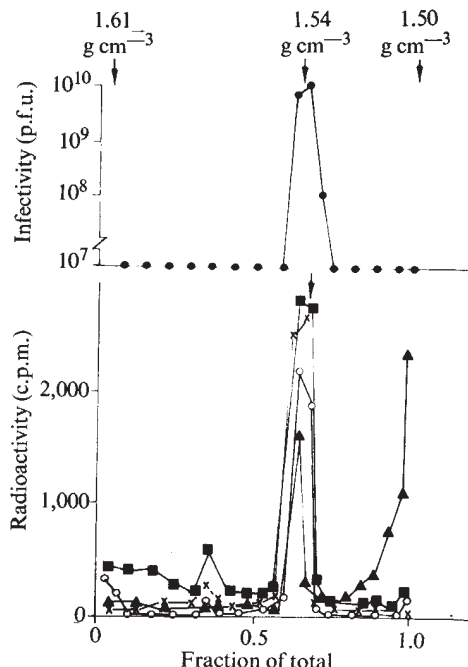


Fig. 1 Banding in caesium chloride of lysates derived from *E. coli* F infected with T5⁺ in the presence of either ³H-thymidine, ³H-leucine or ³H-5-uridine. Bacteria were infected with multiplicity of infection of 7, the cultures were supplemented either with ³H-thymidine (3 μ Ci ml⁻¹), ³H-leucine (0.33 μ Ci ml⁻¹) or ³H-5-uridine (6 μ Ci ml⁻¹). After 60 min aeration each culture received a drop of chloroform. Cell debris was removed by centrifugation and portions of the supernatant fluids were banded in gradients of CsCl. After equilibrium was reached, samples were collected and portions of each (10 μ l.) deposited on to filter disks which were analysed for acid-precipitable radioactivity². Refractive indices of selected fractions were determined and buoyant densities were calculated¹⁶. ●, Infectivity; ○, ▲, and ■, coliphage derived from cultures grown in the presence of ³H-thymidine, ³H-leucine and ³H-5-uridine, respectively; ×, coliphage T5 labelled with ³H-5-uridine after exposure to RNAase (5 μ g ml⁻¹, 37° C, 1 h).

gradient of CsCl allowed recovery of the radioactivity once more in the viral band (Fig. 2).

The head of T5 is porous⁴ and so the uridine could have penetrated into the intact virus. Purified coliphage T5 was therefore incubated with ³H-5-uridine for 20 h at 37° C and the preparation centrifuged to equilibrium in a gradient of CsCl. None of the radioactivity was recoverable in acid-precipitable form in any portion of the gradient. Several preparations of ³H-5-uridine were used and in each case radioactivity cobanded with T5.

Nucleic acids were isolated from several preparations of purified, RNAase-treated T5 derived from cells exposed to

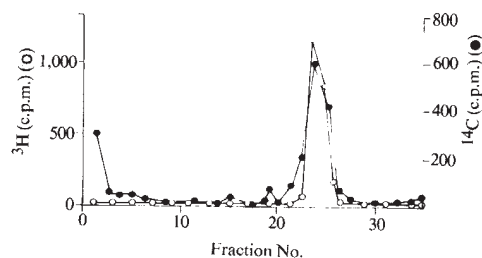


Fig. 2 Rebanding of ³H-5-uridine-labelled coliphage T5 in gradient of CsCl. The peak tubes of the gradient of the ³H-5-uridine-labelled T5 which had been treated with RNAase (Fig. 1) were combined, mixed with ¹⁴C-thymidine-labelled coliphage T5 and run to equilibrium in CsCl. The radioactivity present in the fractions and fraction indices was determined. ○ and ●, Coliphage labelled with ³H-uridine and ¹⁴C-thymidine respectively.

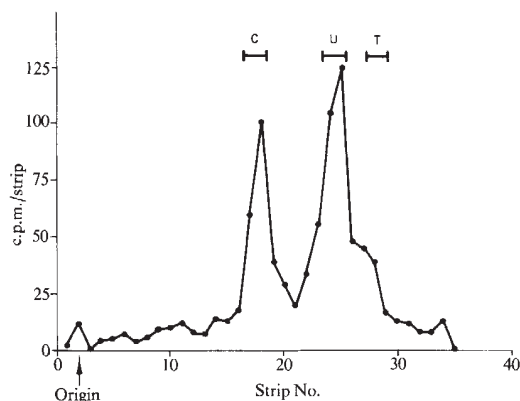


Fig. 3 Distribution of radioactivity among the bases of T5-DNA. "DNA" of T5 was hydrolysed with formic acid¹⁷ and chromatographed on paper with isopropanol: HCl¹⁷. The position of the bases was detected by examination under ultraviolet light. The chromatogram was cut into strips and the radioactivity present thereon determined in a liquid scintillation counter with 10 ml. of omnifluor (4 g l.⁻¹ of toluene). The positions of the individual bases are indicated by lines (C, U, and T; cytosine, uracil and thymine).

³H-5-uridine. The radioactivity of this "DNA" was acid-precipitable (5% trichloroacetic acid), and resistant to digestion by DNAase under conditions which allowed complete digestion of the DNA derived from T5 grown in the presence of ³H-thymidine. On exposure to alkali (1.0 M KOH, 37° C, 18 h) and subsequent reprecipitation with acid, a large portion of the ³H-5-uridine-labelled nucleic acid became acid-soluble, and after incubation with RNAase most of the radioactivity became acid-soluble (Table 1).

Base composition analysis of the ³H-5-uridine-labelled nucleic acid (Fig. 3) showed that the radioactivity was recovered as uracil and cytosine with possibly a small amount as thymine. In a parallel experiment it was found that on hydrolysis of T5-DNA derived from bacteria grown in the presence of ³H-thymidine, the radioactivity was recovered solely as thymine. On the other hand, chromatographic analysis of the ³H-5-uridine-labelled DNA before hydrolysis showed that all of the radioactivity was recoverable at the origin (that is, in higher molecular weight form). Analysis of the ³H-uridine-labelled T5-DNA in gradients of CsCl showed that it had a buoyant density identical to that of T5-DNA labelled with ¹⁴C-thymidine (Fig. 4).

Analysis of the nucleic acids in gradients of caesium sulphate resulted in the ³H-5-uridine-labelled DNA banding at the same position as the control (¹⁴C-thymidine-labelled) T5-DNA. After digestion with DNAase, the control DNA no longer banded but the radioactivity of the ³H-5-uridine-labelled DNA banded at a position typical of RNA (Fig. 5). This band lost its acid-precipitability after digestion with RNAase.

Table 1 Properties of ³H-Labelled T5-DNA

Treatment	Radioactivity retained (c.p.m.)	
	³ H-5-Uridine-labelled	³ H-Thymidine-labelled
None	1,723	2,048
DNAase	1,689	57
RNAase	635	2,033
KOH	228	1,977

Portions of ³H-labelled DNA were diluted in 0.01 M phosphate buffer (pH 7.0) such that the final radioactivity was approximately 2,000 c.p.m. 0.1 ml.⁻¹. Triplicate 0.1-ml. portions were then exposed to DNAase (3 µg, 37° C, 1 h), RNAase (5 µg, 37° C, 1 h) or KOH (1.0 M, 37° C, 18 h). After 1 h the enzyme-treated specimens were acidified with trichloroacetic acid (final concentration, 5%) and processed for the determination of acid-precipitable radioactivity. The sample digested with KOH was neutralized with 1 N HCl and then trichloroacetic acid added.

Our results indicate the ³H-5-uridine is incorporated into the genetic material of coliphage T5, a DNA-containing virus. The alkali lability of the labelled material (Table 1) and its susceptibility to digestion by RNAase following DNAase treatment (Fig. 5) suggest that the bulk of the radioactivity was incorporated into an RNA-like material. The small amount of radioactivity resistant to RNAase and alkali (Table 1) might be due to the conversion of ³H-5-uridine to cytosine and its incorporation into DNA after conversion to deoxycytidine (see Fig. 3).

I suggest that the ³H-uridine is actually incorporated into an RNA-like material because of its ability after DNAase digestion to band in Cs₂SO₄ in the region of the gradient characteristic of RNA. Also this "RNA-like" material is linked to the viral DNA probably covalently because the ³H-5-uridine-label of the "native" material bands in CsCl and Cs₂SO₄ gradients together with the viral DNA.

I do not know the role of this "RNA" in the viral genome, but because one of the DNA strands of T5-DNA contains five interruptions^{5,6}, perhaps the RNA acts to link between these DNA regions or perhaps as initiation sites for RNA polymerase.

In addition to T5-DNA, it has been reported previously that mitochondrial DNA of various origins⁷⁻¹¹, the DNAs of herpes simplex virus¹², *E. coli* 15T⁻¹³ and the colicinogenic factor E₁¹⁴ have been found to be alkali-labile, consistent with the presence of RNA-like material in DNA. Also the DNA

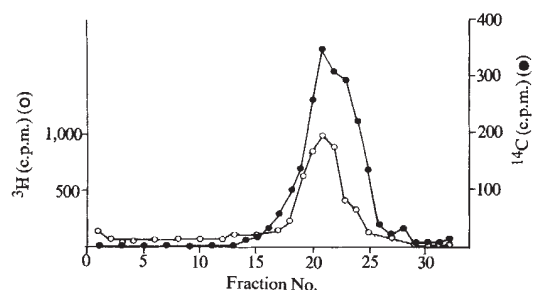


Fig. 4 Banding in CsCl of DNA derived from coliphage T5. Lysates were incubated with DNAase followed by incubation with RNAase, coliphage T5 was then purified by two successive bandings in CsCl, DNA was isolated (phenol procedure). Portions of DNAs derived from ³H-5-uridine and ¹⁴C-thymidine-labelled T5 were mixed and banded in a gradient of CsCl. Acid-precipitable radioactivity present in the fractions was determined.

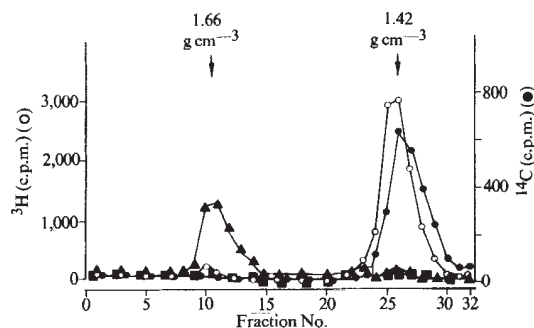


Fig. 5 Banding in caesium sulphate of DNAs derived from coliphage T5. The preparation of the DNA as in Fig. 4. ●, DNA from coliphage T5 grown in the presence of ¹⁴C-thymidine; ○, DNA from T5 grown in presence of ³H-5-uridine. The peak tubes of ³H-5-uridine-labelled DNA were pooled and dialysed against 0.01 M phosphate buffer (pH 7.0) containing 2 × 10⁻³ M MgSO₄. This material was digested with DNAase (1 µg ml.⁻¹, 37° C, 20 min), whereupon a portion of it was incubated further with RNAase (3 µg ml.⁻¹, 37° C, 30 min). ▲, ³H-DNA treated with DNAase; ■, DNAase-treated ³H-DNA subsequently digested with RNAase. Buoyant densities were calculated¹⁸ from the refractive indices.

of the colicinogenic factor E_1 was RNAase sensitive¹⁴. These results suggest that the presence of RNA in DNA may be the reflexion of a basic regulatory mechanism in DNA synthesis (ref. 15).

I am at present attempting to determine the nature of the RNA present in T5 and whether other DNA viruses contain such an RNA.

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Cell-mediated "Immunostimulation" induced by Mammary Tumour Virus-free Balb/c Mammary Tumours

PREHN has advanced the hypothesis that weakly antigenic tumours can lead to a cell-mediated response which stimulates, rather than inhibits, tumour growth¹⁻³. His hypothesis was based on evidence which indicated that a low level immune reaction might enhance tumour growth. Much of this evidence came from experiments using mouse mammary tumours^{1,3}, although the presence of enhancing or blocking antibodies could explain many of the data^{4,5}. Prehn's demonstration that low doses, but not high doses, of specifically sensitized spleen cells could benefit tumour growth in thymectomized, X-irradiated mice provided the first substantial evidence for the immunostimulation theory³.

We have tested the cell-mediated immune stimulation hypothesis directly by using a microcytotoxicity test, which is very sensitive for measuring the effects of lymphocytes and serum from sensitized mice on tumour growth, and has been described by Hellström and Hellström⁶. Briefly, tumour cells from monolayer cultures were plated in a single cell suspension

in wells of a 'Falcon 3040 Microtest II' plate. In these experiments 500 cells were plated per well, and each test involved 8 wells. Following a 24 h incubation period, the medium and cells which had not stuck to the well surface were decanted, and lymph node cells from either normal or sensitized mice were pipetted into the wells. In our experiments the number of lymph node cells added was either 5×10^6 or 5×10^4 per well, giving a ratio of either $10^3:1$ or $10^2:1$ of lymphocytes to tumour cells plated. The plates were incubated for a further 2-3 days, and then the tumour cells which had survived lymphocyte treatment, and therefore still adherent to the surface of the wells, were washed, stained in 2% crystal violet, and counted with the aid of an inverted tissue culture microscope. The number of cells after treatment with normal lymph node cells was compared to that after treatment with sensitized lymph node cells, and the data analysed using the Students *t*-test.

The target tumours used were mammary tumours, free of the mammary tumour virus or any of its variants^{6,7}. These tumours were derived from 2 mammary nodule lines, D1 and D2; line D1 produces only 4% mammary tumours, whereas line D2 produces 50% tumours, by one year after transplantation⁸⁻⁹. The properties and tumour potentials of these lines have been presented in previous reports⁶⁻⁸. All mammary tumours arose from D1 and D2 nodule outgrowths transplanted and maintained in untreated, virgin Balb/cCrgl female mice.

Table 1 Effect of Sensitized Lymphocytes on Syngeneic Mammary Tumours

Target tumours	No. of cells after treatment with lymphocytes from mice immunized to:		
	D1	D2	Control
D1	25.6 ± 3.8*	18.4 ± 3.5	17.3 ± 4.6
D2	6.6 ± 2.8	9.6 ± 4.0†	5.4 ± 2.8
Balb/c C3H	11.9 ± 4.1	11.3 ± 4.3	12.1 ± 3.3
Balb/c MSV‡ tumour	41.3 ± 3.5	43.1 ± 8.1	43.6 ± 12.4

* $P < 0.0025$; % increase = 48%.

† $P < 0.025$; % increase = 78%.

‡ Molony sarcoma virus induced fibrosarcoma.

Several experiments were carried out using tumour tissue as the target cells. In the initial experiment, lymphocytes taken from mice bearing D1 and D2 tumour transplants were tested against D1 and D2 tumour cells *in vitro* (Table 1). Lymphocytes were used at a concentration of 100:1. Sensitized, but not unsensitized, lymphocytes enhanced the growth of specific sensitizing tumours. Growth of other mammary tumours or a MSV induced fibrosarcoma was not influenced by either type of lymphocyte.

The follow-up experiments further documented the phenomena of cell-mediated immunostimulation (Table 2). Lymphocytes were used at ratios of 1000:1 and 100:1. In five of ten experiments, stimulated tumour growth (average increase = 48%) was noted in the presence of sensitized lymphoid cells at a ratio of 100:1 whereas inhibition was seen in none of the ten experiments at this ratio. On the other hand, at a ratio of 1000:1, stimulated tumour growth (average increase, 52%) was seen in two of eight experiments, whereas tumour inhibition (average decrease, 50%) was seen in three out of eight experiments.

Table 2 Effect of Sensitized Lymphocytes on Syngeneic MTV-free Mammary Tumours Tested against Sensitizing Tumours

Type of tumour	No. of experiments CMI* detected		No. of experiments stimulation detected	
	$10^3/1$ †	$10^2/1$ †	$10^3/1$ †	$10^2/1$ †
D1	2/4‡	0/5	0/4	1/5
D2	1/4‡	0/5	2/4	4/5
Total	3/8	0/10	2/8	5/10

* CMI = Cell-mediated inhibition.

† No. of lymph node cells per tumour target cell.

‡ Positives occurred in passage 1 of tumour.

Several points seem to emerge; first, tumours derived from nodule line D2 seem more capable of inducing cell-mediated stimulation than do tumours from line D1 (4/5 vs. 1/5). Second, although cell-mediated inhibition was seen in three out of eight cases, this effect was seen only in first passage tumours. The tumours lost this capacity with serial passage in unsensitized Balb/c mice. For example, lymphocytes from mice bearing a D1 tumour in first passage gave a 31% decrease in tumour growth *in vitro*; in passage 3, no inhibitory or stimulatory effect, and in passage 4, a 48% increase in tumour growth. This observation suggests the importance of using primary or early passage tumours to detect a cell-mediated inhibitory response. Third, cell-mediated inhibition was only detected with a lymphocyte to target ratio of $10^3:1$; stimulation was detected at ratios of $10^2:1$ or $10^3:1$, although more frequently with the lower ratio; and fourth, cross-reactivity was observed between D1 and D2 tumours, more frequently at doses of $10^3:1$ than $10^2:1$ (Table 3). It has also been seen between D1, D2 and MTV-induced mammary tumours at the higher ratio (unpublished data).

Table 3 Effect of Sensitized Lymphocytes on Syngeneic MTV-free Mammary Tumours Tested against Nonsensitizing Tumours

Sensitizing tumour	Target tumour	No. expts. CMI*		No. expts. Stimulation	
		10:3/1†	10:2/1†	10:3/1†	10:2/1†
D1	D2	2/5	0/8	1/5	3/8
D2	D1	0/2	0/4	2/2	0/4
Total		2/7	0/12	3/7	3/12

* CMI = Cell-mediated inhibition.

† No. of lymph node cells per tumour target cell.

Cross-reactivity suggests the presence of an organ-specific or possibly nodule-specific, rather than tumour-specific, antigen. The presence of organ-specific antigens has been postulated by Weiss *et al.*⁹ on the basis of the ability of lactating mammary gland to immunize against D1 and D2 mammary tumour growth. It is of interest that they also found that pre-immunization led to enhanced growth *in vivo* of D1 and D2 tumours, a situation in keeping with the *in vitro* data reported here.

Preliminary studies show that serum taken from sensitized mice bearing D1 and D2 tumours can sometimes block the stimulation effect (G. H. and D. M., unpublished results). The experiments presented here, however, demonstrate clearly that lymphocytes from tumour-sensitized hosts can show "enhancement" or stimulation of tumour growth. These data support the hypothesis by Prehn that weakly antigenic tumours, in this case virus-free Balb/c mammary tumours (ref 9; and D. M., unpublished results), elicit a cellular immune reaction that stimulates tumour growth. The significance of this phenomenon has important implications for understanding the role of the immune system in neoplasia, and in particular for understanding such phenomena as "sneaking through", immunosurveillance, and the immunological significance of weakly antigenic tumours.

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Chromosome Pairing

IN a useful article which appeared under this title recently¹ H. L. K. W. says at one stage: "Nothing is known about the mechanism of chromosome pairing at the molecular level, but Watson and Crick (*Nature*, **171**, 964; 1953) suggested that it involved the pairing of complementary nucleotide chains to form a double helix. There seems to be no alternative to this account for the specificity of pairing, and a more detailed hypothesis along these lines has been proposed by Sobell (*Proc. US Nat. Acad. Sci.*, **69**, 2483; 1972)".

To me, there at least "seems to be an alternative" in the form of a model in which two homologous double helices of the Watson-Crick type are paired specifically about a dyad axis coincident with their long molecular axes^{2,3}.

A similar mechanism of pairing might also be involved in the formation of tertiary structure in the nucleic acid of chromosomes where repeated, perhaps particularly reverse tandem, base pair sequences occur.

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Diphtheria Toxin: Specific Competition for Cell Receptors

DIPHTHERIA toxin causes the catalytic inactivation of polypeptide chain Elongation Factor 2 when the enzymically active N-terminal fragments of toxin, particularly fragment A, are mixed with broken cells of almost any eukaryotic source¹⁻³ or when complete toxin molecules are incubated with intact susceptible cells⁴. Incubation of intact cells with fragment A does not lead to EF-2 inactivation. Probably, therefore, an apparatus exists in the membranes of susceptible cells that facilitates the uptake of toxin and generation of its fragment A in the cytoplasm and the entry process involves the C-terminal portion of the toxin molecule, fragment B (ref. 5).

Uchida *et al.*⁶ have described the product of a mutant toxin gene, *crm*₁₉₇, a non-toxic protein of the same molecular weight as toxin which has an apparently normal fragment B but an enzymically inactive fragment A. Because *crm*₁₉₇ reduces the effect of toxin on HeLa cells and yet has no effect on the reaction catalysed by fragment A *in vitro*, Uchida *et al.* suggested that *crm*₁₉₇ might compete with toxin for sites on the cell membranes.

We now show by dose-ratio analysis that the inhibition can indeed be described as competitive. Typical HeLa cell dose-response curves for toxin alone and with *crm*₁₉₇ are shown in

Fig. 1. As expected for competitive inhibition, the curves are similar in shape and reach the same maximum⁷. From each of several such pairs of curves, obtained with crm_{197} concentrations (I') from 1 to 32 $\mu\text{g ml}^{-1}$, we determined values of toxin concentrations required to give the same response in the presence (T') and in the absence (T) of the inhibitor (Fig. 2).

The linear relationship between $\log \left(\frac{T'}{T} - 1 \right)$ and $\log I'$, with a slope of unity, is the result expected if toxin and crm_{197} compete for a common cellular target, because in such situations the following relationship holds $\left(\frac{T'}{T} - 1 \right) = \frac{I'}{K_I}$ (ref. 7). The intercept

indicates that the apparent dissociation constant (K_I) of the crm_{197} target complex is about 10^{-8} M.

Crm_{197} also protects rabbits and guinea-pigs against the local necrotic action of toxin injected into the skin. A very high ratio of crm_{197} to toxin is required because the skin responds to extremely little toxin and yet protection can only be significant when the crm_{197} concentration is of the same order as its dissociation constant.

In the rabbit the situation is slightly confused by a separate reaction given by these relatively high concentrations of crm_{197} alone. The normal rabbit response 2 day after the intradermal injection of 40 μg of toxin is a red patch about the same size as the bleb raised on injection (8–10 mm diameter). Larger doses give a larger red area which may have a haemorrhagic and necrotic centre. These reactions are completely suppressed by sufficient amounts of crm_{197} . But crm_{197} alone sometimes provokes a pale red ring with an internal diameter of 15–20 mm and this is intensified by toxin. In such cases, protection is more obvious two weeks after injection when the rings given by crm_{197} alone have faded.

Heat denatured crm_{197} does not protect cells *in vivo* or in culture against the action of toxin.

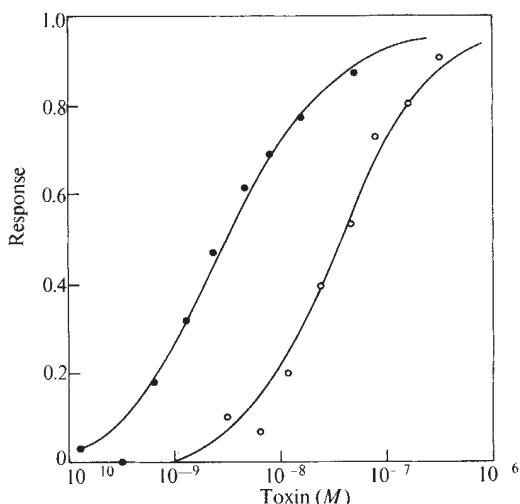


Fig. 1 HeLa cell dose-response curves for toxin (●) and toxin in the presence of 20 $\mu\text{g ml}^{-1}$ of crm_{197} (○). Cells growing exponentially in spinner culture were collected by centrifugation and resuspended to 5×10^6 cells ml^{-1} in Eagle's Minimum Essential Medium supplemented with 2% foetal calf serum. 1.5 ml. aliquots of the suspension were measured into 15 ml. plastic conical tubes (Falcon) containing various amounts of toxin and crm_{197} and incubated in a 37° C water bath with moderate shaking. After 2.5 h, 0.5 μCi of [^{14}C]-L-leucine (312 Ci mol^{-1}) was added to each tube. One hour later the cells were chilled, collected on glass fibre filters and washed with 0.15 M NaCl to remove serum proteins and then with 5% trichloroacetic acid. The filters were dried and counted by liquid scintillation. The response of cells was computed as $(C - C')/C$ where C' is c.p.m. incorporated in the presence of toxin and C the control in the absence of toxin. C was generally about 7,000 c.p.m. incorporated per hour and this rate of incorporation was constant for at least 4 h after the cells were transferred to plastic tubes, even though they tended to settle.

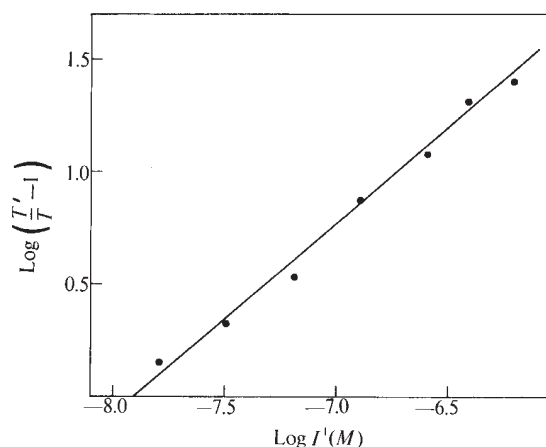


Fig. 2 Schild plot of the antagonism by crm_{197} of the action of toxin in HeLa cells. Dose ratios (T'/T) were calculated at response level 0.4 from pairs of dose-response curves such as those shown in Fig. 1.

All these observations might also be explained if crm_{197} acted, not as a competitive inhibitor, but by combining with toxin and neutralizing it⁹. We consider this neutralization unlikely because crm_{197} does not inhibit the enzymic action of fragment A *in vitro*; dimers¹⁰ and higher aggregates of toxin are toxic; and a mixture of 10^{-7} M toxin and 4×10^{-6} M crm_{197} , at which concentration there would be almost complete protection in HeLa cell cultures, produces a response in rat skin indistinguishable from that with toxin alone. Rat cells seem to lack the specific mechanism for toxin uptake existing in sensitive cells and yet can be intoxicated by comparatively very high concentrations of toxin which appears to enter cells very slowly⁹ by a non-specific route (T. J. and J. M. Moehring, personal communication).

Thus, we believe that the present evidence shows true competition between toxin and crm_{197} for some cellular receptor. The results do not locate the receptor unambiguously but it is clearly most likely to be a component of the cell membrane involved with the initial binding of toxin or its subsequent entry into the cytoplasm. Because fragment B is necessary both for entry and for competitive inhibition, it is reasonable to suppose that the binding of toxin or crm_{197} to the receptor occurs primarily through fragment B. Thus, the dissociation constant, about 10^{-8} M, found for crm_{197} would be identical to that of toxin itself. A constant of this magnitude would explain the level of the so-called "saturating dose" of toxin, the lowest concentration that gives the most rapid inhibition of protein synthesis in tissue culture cells. For HeLa cells this is about $2-3 \times 10^{-8}$ M (refs. 11, 12) at which most of the receptors would be occupied and the addition of more toxin could have little extra effect.

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Senescence of Human Cells in Culture

DR L. K. BLEYMAN¹ need not be concerned that our experiments on clonal senescence of human cells in culture are being carried out in ignorance of earlier studies of such ageing in protozoa. Indeed the paper he cites² refers to one important study carried out with protozoa. The experiments with human cells are derived directly from earlier work with simple eukaryotic organisms such as fungi. When the first results were being prepared for publication³, reference was made to related studies with ciliated protozoa and a copy was sent to Professor T. M. Sonneborn for comment. In subsequent correspondence with him it became clear that it would not be possible (in a paper limited in length by the editor of *Nature*) to do justice to the many important observations on the complex interaction between nuclear and cytoplasmic degenerative changes during ageing in these organisms. It would be most valuable if Dr Bleyman could now be persuaded to publish a review of these experiments in the light of subsequent biochemical studies on the mechanism of clonal senescence in other organisms.

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Circadian Variation of the Lethality of Methadone

Lenox and Frazier¹ have reported the discovery of a circadian variation of methadone tolerance in rats. Their claim hinges on an observed survival of nine out of twenty-six rats (34.6%) injected at 0500 h compared to an average survival of only 17.3% for similar groups injected at five other times of day. But their use of the χ^2 test is incorrect and the experimental results do not support the hypothesis that the circadian cycle influences the tolerance to methadone.

To calculate the significance of the observed variation of survival percentage with time of injection it is necessary to recognize that survival statistics in experiments with small groups are neither Gaussian nor Poisson, but are binomial². Whenever an experiment with a group of size n has only two possible outcomes (such as survival and death) with probabilities p and q ($q = 1 - p$) the probability of x survivals is given by

$$P(x) = n!(x!(n-x)!)^{-1}p^xq^{n-x}$$

The best estimate of p , under the null hypothesis that the survival rate is independent of time of injection, is defined by the observed survival of 31 animals out of the 153 used in the programme of six experiments. Therefore $p = 0.203$ and $q = 0.797$. The binomial function based on these values for p and q , with $n = 26$, as for the group at 0500 h, is shown in Fig. 1. The sum of the ordinates from $x = 0$ to $x = 8$ is equal to 0.936

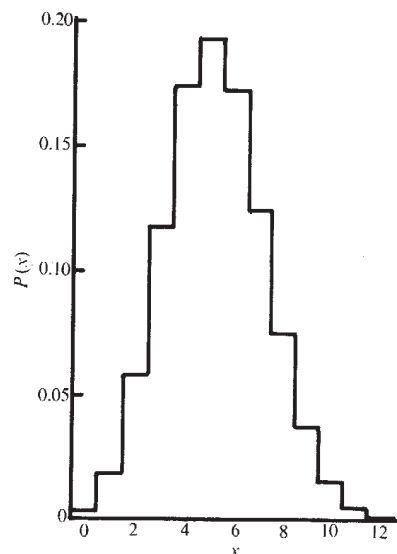


Fig. 1 The binomial function for $n=26$ and $p=0.203$.

and therefore the likelihood of 9 or more survivals is 6.4% in this one group. But there were five other groups, any one of which could have produced an interesting result. The probability of obtaining eight or fewer survivals in all six groups is equal to the product of the six separate probabilities. There are only two distinct probabilities to consider: 0.936 for $n=26$ in three experiments and 0.950 for $n=25$ in the other three. The overall probability that $x < 9$ is therefore $0.936^3 \times 0.950^3 = 0.703$. It follows that there will be a 29.7% chance that $x > 8$ in at least one of the six groups, and the null hypothesis is compatible with the observations.

Statistical interpretation of the results of this experiment is complicated by the fact that previous work cited by Lenox and Frazier had suggested that survival would be greatest at 0900 h, only one time interval away from the 0500 h group. If the work is repeated it will require only eight survivals at 0500 h or 0900 h to rule out the null hypothesis.

Unless there are compelling biological reasons for using an LD_{50} dose of methadone the sensitivity of the experiment can be doubled by employing the drug at the LD_{50} level.

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Attraction of *Spodoptera littoralis* Larvae to Colours

DURING a research programme on phagostimulants¹⁻³ for the larva of the Egyptian cotton leafworm, *Spodoptera littoralis* Bois., it was found that their incorporation into poison baits did not sufficiently improve the latter's attractivity. Further stimuli, for example optical ones, seemed to be needed. We therefore determined the influence of edible colours, similar to those used in studying boll weevil attraction⁴, on the feeding rate of *S. littoralis*. A range of commercial food colours of the 'Edicol Supra' and 'Edilake' ranges (Imperial Chemical Industries, England), now produced under the label of 'Certicol' and 'Certolakes', respectively (Williams (Hounslow) Ltd), were tested. The 'Edilake (Certolake)' colours are aluminium lakes containing a high proportion of alumina as extender of the corresponding 'Edicol Supra (Certicol)' dyes, which are sodium

Table 1 Colour Attraction in Phagostimulation Trials with *Spodoptera littoralis* Larvae

No.	Hue	Methuen notation*	Name of colour	Feeding ratios† at dye concentration tested	
				1%	0.25%
1	Yellow	2A6	'Edicol Supra Tartrazine NS'	0.96	2.1
2	Yellow	3A4	'Edilake Tartrazine NS'	1.9	2.1
3	Yellow	3A4	'Edilake Yellow FCS'	3.3	2.0
4	Orange yellow	4A6	'Edicol Supra Yellow N'	0.61	2.4
5	Orange	5B2	'Certolake Plain Chocolate Colour 175290'	2.1	
6	Orange	5B3	'Certolake Milk Chocolate Colour 175285'	1.8	
7	Orange	6A6	'Edicol Supra Yellow FCS'	0.65	4.9
8	Reddish orange	7A5	'Edicol Supra Orange AG'	1.1	2.2
9	Red	9A5	'Edicol Supra Ponceau 4RS'	0.25	0.94
10	Red	10A4	'Certolake Ponceau 4R'	1.4	
11	Red	11B4	'Edicol Supra Carmoisine WS'	0.55	0.93
12	Red	11B5	'Edicol Supra Raspberry A'	0.77	1.1
13	Bluish red	12B5	'Edicol Supra Amaranth AS'	0.34	0.84
14	Bluish red-purple	12C3	'Edicol Supra Blackcurrant A'	0.44	1.4
15	Purplish red	13A6	'Edicol Supra Erythrosine'	0.25	0.36
16	Purplish red	13A5	'Certolake Erythrosine'	0.76	
17	Purplish red	13-14B4	'Certolake Amaranth'	1.4	
18	Blue	21B4	'Edicol Supra Blue XS'	0.6	0.59
19	Blue	22A4	'Certolake Indigo Carmine'	1.3	
20	Blue	23A7	'Edicol Supra Blue EGS'	0.16	0.41
21	Turquoise	24C8	'Certicol Green S'	2.3	1.7
22	Green	27B4	'Certolake Green 172257'	4.4	1.7
23	Green	27B4	'Certolake Green 172679'	2.1	

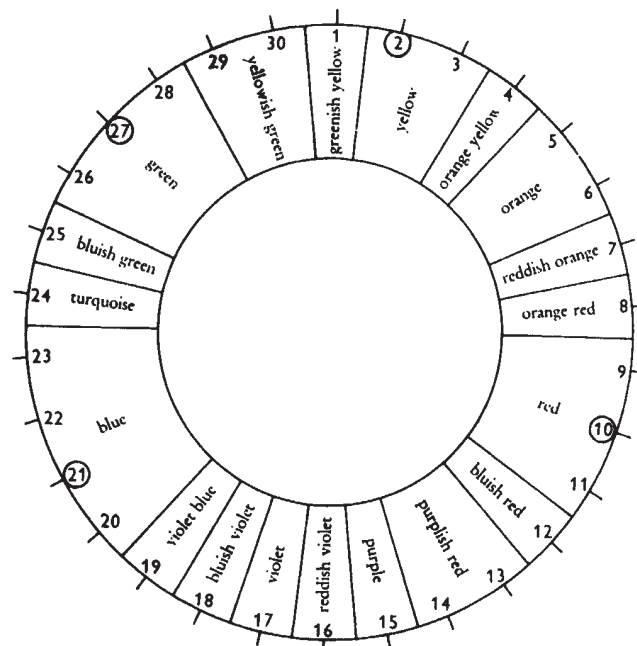
* The colour of 'Edicols' and 'Certicols' was determined according to the *Methuen Handbook of Colour*⁵, on 'Styropor' lamellae painted with 0.25% of the dye, whereas 'Edilakes' and 'Certolakes' were determined at 1%.

† The ratio of weight 'Styropor' consumed in choice trials (lamellae treated with dyes + 3% sucrose tested against lamellae treated with 3% sucrose alone) is recorded in the last two columns, feeding ratios.

The average total consumption on two lamellae in these experiments was 8.6 mg.

salts. 'Edilakes' are used mainly when water-soluble food colours would be unsuitable, for example in fatty or oily media, and contain generally from 15 to 25% of the corresponding 'Edicols'.

To assess phagostimulation, we used the 'Styropor method'¹; lamellae (6×3 cm) of 'Styropor' (foamed polystyrene) of density 0.016 (P₁₆), with dry sucrose residues as phagostimulant,

**Fig. 1** The colour circle⁵. The numbers which represent the four primary colours have been ringed.

were offered in large Petri dishes (15 cm) to larvae of *S. littoralis* weighing 170–190 mg, under ordinary day-and-night conditions of illumination and at 27° C. In this study the lamellae were painted with varying sucrose and dye concentrations in water-ethanol 9:1, containing one drop of 'Triton X-100' per 10 ml. of solution as spreader, and were left to dry for 24 h. Both choice trials (two differently treated lamellae per dish) and no-choice trials (only one lamella per dish) were conducted. The weight of 'Styropor' consumed per larva served as criterion of phagostimulation, the results being recorded after 48 h.

In choice trials between lamellae treated with 3% sucrose plus varying concentrations of dyes compared with 3% sucrose only, it was found that the larvae feed more strongly on certain of the coloured lamellae (Table 1). In fact, all the colours lying in a semicircle, ranging clockwise from turquoise (24) to reddish orange (7) in the colour circle (Fig. 1), enhanced phagostimulation; this is the area around the primary colours green and yellow⁵. Colours lying within the other half of the colour circle (around the primary colours red and blue) were inactive or even repellent (Table 1).

In the attractant colours, colour intensity also played a role: colours which are too intensive were less attractive. Activity was therefore mostly higher with 'Edicols' at 0.25% than at 1%;

Table 2 Choice Trials with Two Yellow and One Green Colour

Dye			Sucrose	versus	Dye			Sucrose	Feeding ratio
A	1% 'Edilake Yellow FCS'	+	3%		1% 'Edilake Tartrazine NS'	+	3%	1.0	
	1% 'Edilake Yellow FCS'	+	3%		1% 'Certolake Green 172257'	+	3%	1.8	
	1% 'Edicol Supra Tartrazine NS'	+	3%		1% 'Certicol Green S'	+	3%	1.8	
B	1% 'Edilake Yellow FCS'	+	3%		—		5%	0.96	
	1% 'Edilake Yellow FCS'	+	3%		—		6%	0.65	
	1% 'Edilake Yellow FCS'	+	3%		—		7%	0.57	
	1% 'Edilake Yellow FCS'	+	3%		—		8%	0.56	
	1% 'Edilake Tartrazine NS'	+	3%		—		5%	0.96	
	1% 'Certolake Green 172257'	+	3%		—		5%	1.0	
	1% 'Certolake Green 172257'	+	3%		—		8%	0.51	
	Controls: —		3%		—		3%	1.0	
	—		3%		—		5%	0.52	
	—		3%		—		8%	0.33	

A: Colour + 3% sucrose against another colour + 3% sucrose.

B: Colour + 3% sucrose against varying concentrations of sucrose.

the 'Edilakes' were highly active at 1% as they contain only a quarter or less of the corresponding 'Edicol'.

In choice trials between yellow and green colours applied on sucrose-treated 'Styropor' lamellae (Table 2, A), two 'Edilake' yellow colours, 'Yellow FCS' and 'Tartrazine', were equally active, but much more attractive than 'Certolake Green 172257'. This is interesting because in no-choice experiments this green dye was consistently more attractive than the yellow lakes. As 'Certolake Green 172257' is a mixture based on 'Certicol Green S' and 'Certicol Tartrazine S' ('Edicol Supra Tartrazine NS'), we tested these two constituents against each other. The yellow colour was again the more attractive.

Sucrose (3%) with 1% of 'Edilake Yellow FCS', 'Edilake Tartrazine NS' or 'Certolake Green 172257' were about equally phagostimulatory to 5% sucrose (Table 2, B), resembling Wiesmann's classical red hue colour experiments⁶ (water-wetted red filter paper disks were as attractive to houseflies as 1–5% sucrose solutions soaked into white filter paper disks). The table also shows that 3% sucrose was half as active as 5%, but when fortified with 1% dye it was half as active as 8% sucrose.

Table 3 No-Choice Trials with Yellow and Green Colours

Sucrose	Colour	'Styropor' lamella consumed mg/larva
3% +	1% 'Edilake Tartrazine NS'	7.2
—	1% 'Edilake Tartrazine NS'	1.1
3% +	1% 'Edilake Yellow FCS'	5.2
—	1% 'Edilake Yellow FCS'	0.4
3% +	1% 'Certolake Green 172257'	9.6
—	1% 'Certolake Green 172257'	0.7
3%	—	6.8

The approximate equality of attraction between 5% sucrose and 3% sucrose with 1% of either of the two yellow dyes or the green dye does not imply that 1% of the dyes alone is equivalent as phagostimulant to 2% sucrose; they are non-phagostimulatory alone at this concentration (Table 3). This could also be inferred from observations every 10 min in 5-h-long choice experiments, during which the frequency larvae stayed on either the 1% 'Edilake Tartrazine NS' or the 3% sucrose lamella was determined. Larvae stayed about twice the time on the 'Edilake Tartrazine NS' as on the sucrose lamellae, but fed almost exclusively on the latter. The dye seems thus to be an arrestant⁷ for larvae of *S. littoralis*. This conclusion is supported by the finding that the positive bias conferred by 1% 'Edilake Tartrazine NS' to 3% sucrose, compared to 3% sucrose alone, disappears when such choice experiments are conducted in complete darkness.

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Vascular Permeability Factor: Dissociation from the Angiotensin II Induced Pressor and Drinking Responses

THE parenteral administration of saline extracts of renal tissue to nephrectomized animals of various species causes protracted elevation of blood pressure, increased drinking, formation of ascites and pleural effusions, and arteriolar necrosis^{1–7}. While renin has been implicated in pathogenesis as it is a major component of saline renal extracts, the mechanisms producing these various phenomena and their interrelationship remain unclear. It has been postulated^{5,6} that the blood pressure response is due to angiotensin II generated by the renin-rich extract and the effusions caused by changes in vascular permeability induced by the blood pressure elevation. Asscher⁷, however, suggested that another factor of renal origin was involved which increased vascular permeability to plasma proteins.

Considerable evidence has already been accumulated to support the theory that excess renin, by angiotensin formation, is vasculotoxic. Animals with renal artery clipping who develop malignant hypertension do have excessive renin and aldosterone secretion⁸, and the simultaneous administration of these hormones can produce devastating vascular injury and serous effusions⁹. Furthermore, diffuse myocardial and renal lesions can be produced by administration of large doses of angiotensin¹⁰. The vasculotoxicity of renin is also suggested by its presence in excessive amounts in human malignant¹¹ and renovascular hypertension and by the direct relationship between peripheral plasma renin activity and vascular complications in patients with essential hypertension¹².

The recent synthesis of a highly specific peptide competitive inhibitor of angiotensin II, Sarcosine¹ Ala⁸ angiotensin II¹³ enables investigation of vascular permeability subsequent to intraperitoneal injection of crude renal extract in the presence of angiotensin blockade. We used this approach to clarify the role of excess renin and angiotensin in causing vascular permeability.

Female Wistar rats (295 to 325 mg) were bilaterally nephrectomized. The femoral vein was cannulated for infusion

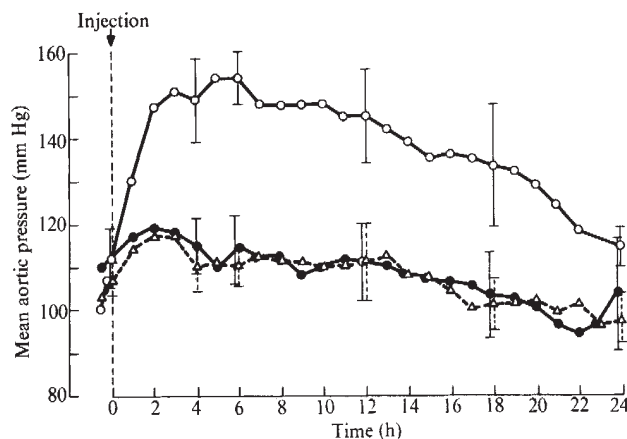


Fig. 1 Infusion of an angiotensin II inhibitor in nephrectomized rats completely blocked the characteristic protracted pressor response induced by the intraperitoneal injection of crude renal extracts. (Mean $\pm$ s.d.) (○—○, Renal extract; ●—●, renal extract and inhibitor; △---△, saline.)

and the external iliac artery for constant blood pressure monitoring while the animal was awake and drinking. The kidneys were homogenized with 5 ml. of 0.9% saline in a 'Vertis' blender, and the homogenate was centrifuged at 5,000 r.p.m. for 10 min. Two gram liver aliquots obtained from other animals were similarly prepared. Following blood pressure stabilization, 3.5 ml. of either saline (N-6), or the supernatant from the renal extract (N-5), or liver extract (N-8) was injected intraperitoneally with a blunt needle.

In an additional six animals, intravenous infusion of the angiotensin inhibitor at $4 \mu\text{g min}^{-1}$ completely blocked the pressor response to an intravenous dose of 100 ng angiotensin II. Kidney extracts were then injected and the infusion of the blocker was continued throughout the study. Complete blockade of the pressor effect of intravenous exogenous angiotensin II was reaffirmed at 4, 12 and 24 h.

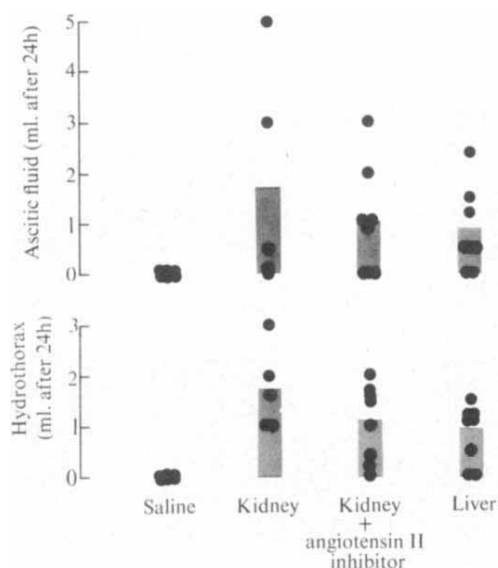


Fig. 2 Intraperitoneal injections of either crude renal or hepatic extracts produced pleural and abdominal effusions in nephrectomized rats. Concurrent infusion of the angiotensin II inhibitor did not prevent the fluid accumulation produced by the renal extracts.

Intraperitoneal administration of the crude renal extracts produced an immediate and sustained rise in blood pressure (Fig. 1) which was significantly elevated above control in 1 h ($P < 0.01$). Blood pressure reached peak levels at 6 h (154 ± 4.5 mm Hg s.d.) and then fell slowly over the remaining 24 h period. In contrast, in animals given the saline injection, the blood pressure did not rise significantly above baseline. The pressor response of the crude renal extract was totally abolished in animals receiving infusion of the angiotensin II inhibitor.

A second effect of the crude renal extracts was to stimulate drinking. The fluid intake over the 24 h period (31 ± 10 ml. s.d.) in these animals was significantly greater ($P < 0.01$) than in the animals with the saline injection (10.4 ± 6.0 ml.) or those given the liver extract (10 ± 5.3 ml.). Increased drinking was similarly abolished by administration of the angiotensin II inhibitor. Fluid intake in the animals given the inhibitor and the crude renal extract (15.8 ± 4.4 ml.) was not significantly different from either the control saline group or the group given liver extract.

In contrast, the induction of serous peritoneal and pleural effusion was not suppressed by the angiotensin inhibitor (Fig. 2). Thus, this response does not seem to be the result of the pressor action of the generated angiotensin II. Heterologous liver extract studies enable the pressure response to be dissociated from the production of serous effusions. Although the liver extracts caused neither hypertension nor

drinking, they did produce serous effusions in seven of eight animals.

Our results confirm that the hypertension and drinking responses in nephrectomized rats after intraperitoneal injection of renal extracts are mediated by the generation of angiotensin II as they were both entirely abolished by a specific angiotensin inhibitor. In contrast, it does not seem to be the factor involved in the production of serous effusions, the so-called vascular permeability factor; effusions occurred during angiotensin blockade and were also caused by liver extracts. Although production of severe hypertension in rats may be associated with areas of constriction and dilatation of small arteries resulting in sequestration of plasma proteins beneath the endothelium¹⁴, an elevated blood pressure *per se* was not a prerequisite for serous effusion formation and no vascular lesions were found on histological examination. We suggest that the occurrence of serous effusions observed in animals receiving renal extracts is not dependent on hypertension-induced vascular damage.

Our results agree with those of Giese⁴ and Nairn³ in which angiotensin II infusions did not produce a serous effusion to the same extent as intraperitoneal injection of renal extracts in nephrectomized rats. Suggestions that the effusions are due either to an unidentified renal substance causing changes in vascular permeability⁷ or to a renin effect other than generation of angiotensin II⁶ are rendered less likely by our findings of similar effusions after injection of liver extracts. They are more likely to be due to a non-specific effect of tissue proteolytic enzymes and other products injected into the peritoneal cavity. Furthermore, Asscher¹⁵ has demonstrated that non-pressor placental extracts also produce serous effusions.

Angiotensin II can produce vascular injury¹⁶, but the pleural or peritoneal effusions often observed after injection of renal extracts²⁻⁷ or with bilateral ureteral occlusion¹⁷ do not seem to be a specific consequence of its action. On the other hand, our study reaffirms the specificity of angiotensin II as the pressor and polydipsic agent occurring in renal extracts.

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Liquid Crystals in Human Bile

GALLSTONES may grow from microspheruliths, non-crystalline associations of cholesterol, pigment or calcium carbonate^{1,2}; these spherical structures have been observed to aggregate and crystallize, but their composition and nature have never been well defined.

Bourges *et al.*³ and Admirand and Small⁴ have largely excluded para-crystalline phases in the mechanism of cholesterol precipitation. The results of Admirand and Small⁴ suggest that human bile is either a one or two phase system (micellar solution or micellar solution plus crystalline cholesterol). A stable three-phase system (crystalline, liquid crystalline and micellar) could occur at unusually high lecithin concentrations. When the maximum cholesterol solubility limit has been exceeded therefore, crystalline cholesterol is expected to precipitate from bile.

We have observed as much cholesterol above saturation in normal, non-gallstone associated, biles as in patients with cholelithiasis, yet only the latter group may have solid crystals. We therefore re-examined the morphology of biliary precipitates, particularly the formation of birefringent particles as detected by polarizing microscopy.

Eleven cholesterol gallstone-associated samples were studied soon after collection with the temperature maintained at 37° C; other specimens had been stored at -20° C. In all, twelve specimens of normal bile and forty-six of gallstone-associated bile were examined.

The birefringent particles seen were of two types. Small solid crystals in the form of parallelepipeds (cholesterol crystals) were found in fresh lithogenic specimens and stored specimens of normal and abnormal samples. Also, birefringent droplets with a diameter of about 5 μ m were frequently observed, which decreased in number on heating from room temperature to 37°-40° C, and disappeared completely at even higher temperatures.

The droplets often formed clusters as shown in Fig. 1. Large birefringent areas formed from slow coalescence at room temperature (Fig. 2). Occasionally, areas with a pseudo-isotropic texture developed which were optically positive uniaxial. The batonnets in Fig. 3 resulted from rapid cooling of a sample which had been heated to 80° C. These features indicate a liquid crystal state with a lamellar structure⁵⁻⁷. Liquid crystalline mesophases have been reported in other body fluids and normal tissues, for example, plasma of humans with hyperlipaemia⁸ and biliary obstruction⁹; and adrenal cells, ovary and muscle⁸.

To verify the liquid properties of the droplets, some samples were passed through a 0.025 μ m pore size microfilter. As the filtrate still contained droplets of much larger diameter, these can be deformed and flow through very narrow openings.

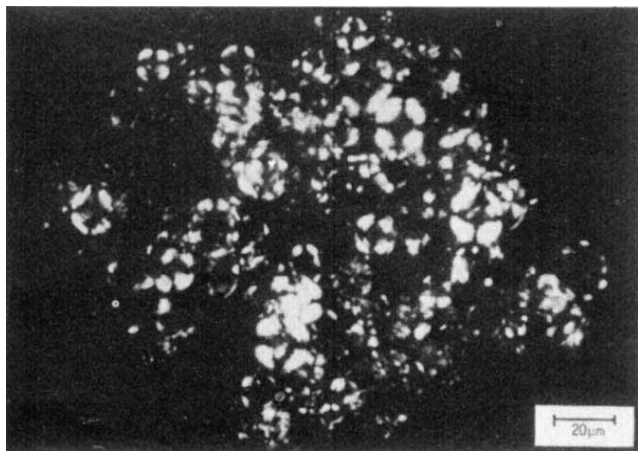


Fig. 1 Liquid crystal spherulites, untreated human bile at 23° C, crossed polarizers.

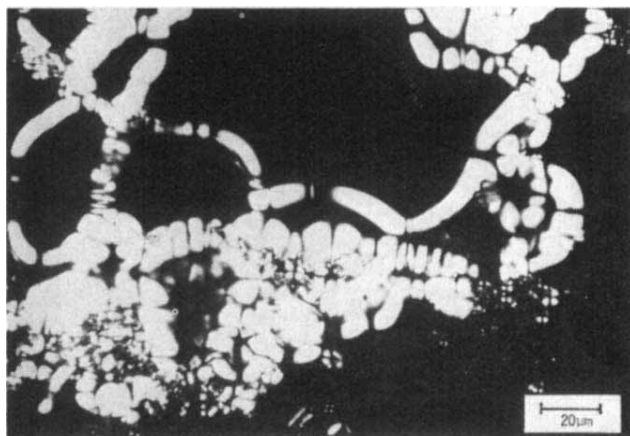


Fig. 2 Extended liquid crystalline areas. 23° C, crossed polarizers.

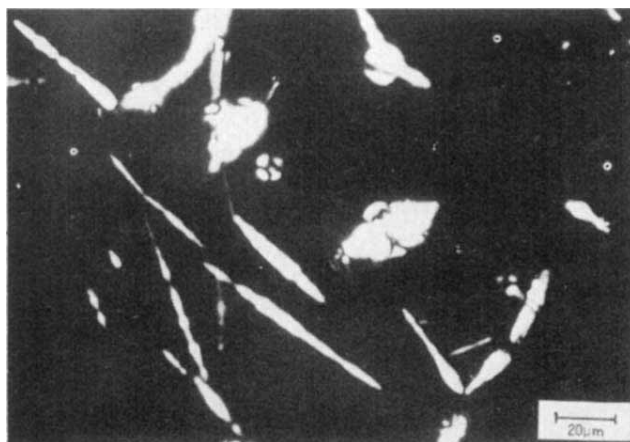


Fig. 3 "Batonnets" obtained by heating to 80° C and successive cooling. 23° C, crossed polarizers.

We observed liquid crystals in eleven fresh lithogenic biles and twenty-four stored bile samples of which five were normal and nineteen were associated with gallstones. All samples were saturated or supersaturated with cholesterol (saturation defined in ref. 10). In the detailed study on human bile by Admirand and Small⁴, microscopic observations were confined to the centrifugation sediment, in which only solids were found. This would be expected in view of our observation that the liquid crystals are less dense than bile and, therefore, float on centrifugation.

The liquid crystalline state in human bile seems not to be stable. Sequential microscopic observations of human biles maintained at 37° C for as long as two weeks showed that the liquid crystal particles slowly disappear and cholesterol crystals form in compensation. They completely disappeared in a sample that initially showed only liquid crystals, for example, within 72 hours after incubation at 37° C, and cholesterol microcrystals were formed instead.

As the composition of the liquid crystals has not been determined, their role in gallstone formation cannot yet be defined. We suggest that the cholesterol concentration in the liquid crystalline phase is considerably higher than in the surrounding isotropic phase, and the presence of liquid crystals inhibits the precipitation of excess cholesterol in a solid crystalline form by delaying its nucleation. This would result from reduction in cholesterol supersaturation in the micellar phase by the formation of a liquid crystalline portion with a relatively high cholesterol concentration.

A stabilizing influence of liquid crystals depends upon their more rapid nucleation than solid crystals. We observed only

liquid crystals in fresh specimens of human bile, which supports this hypothesis. The small size of the liquid crystals suggests simultaneous nucleation at a large number of sites. A rapid change from a stable to an unstable solution leading to multiple nucleation could result from diurnal variations in the composition of hepatic bile both in man^{11,12} and in other primates¹³. Liquid crystals in human bile may thus play an important role in the transition from the non-lithogenic to the lithogenic state. Further studies of this complex and dynamic system are necessary in regard to compositional changes and time scales.

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Toxicology of Fluoro-olefins

THE often surprising toxicity of several of the fluorinated organic compounds is well known¹. A number of rather diverse structural types have been found to impart high toxicity although seemingly closely related types have been found to have rather low toxicities. Unfortunately, this varied behaviour of fluorinated compounds has occasionally become tragically established. While the *modus operandi* is now known for types such as monofluorides², phosphofluoridates³, and active halogen compounds, for example, α -haloketones, much less is understood about fluorinated alkenes⁴.

This toxicity, or lack of it, has seemed to be bestowed upon fluoro-olefins in a random fashion. Attempts to correlate trends in toxicity with increasing fluorine substitution by ascribing olefin hydrolysis to hydrogen fluoride have not been entirely satisfactory. For example, perfluorobutene-2 and perfluoroisobutylene are isomeric, but although the toxicity of perfluoroisobutylene is well known, perfluorobutene-2 is not considered especially dangerous. Also, chlorotrifluoroethylene is about forty times more toxic than tetrafluoroethylene, and perfluoroisobutylene is about ten times as toxic as phosgene although both would be expected to be similar if hydrolysis were the only causative agent. One particularly interesting finding is the three-fold higher toxicity of *trans*-2,3-dichlorohexafluorobutene-2 over that for the *cis* isomer⁵.

Table 1 Olefin Toxicities

Olefin	LC ₅₀ , p.p.m. (4 h exposure)	ALC, p.p.m.
CH ₂ =CHF		800,000
CH ₂ =CF ₂		128,000
CF ₂ =CF ₂	40,000	
CH ₂ =CCl ₂	32,000	
CHCl=CCl ₂		8,000
CCl ₂ =CCl ₂		4,000
CF ₃ CF=CF ₂	3,000	
	(3,240 to 13,365; 2 h)	
CF ₂ =CFCI	1,000	
	(7,560; 2 h)	
CF ₂ =CCl ₂		1,000
CF ₃ CF=CHCF ₃		200
CF ₃ CCl=CClCF ₃		100
<i>trans</i>	(61; 1 h)	
<i>cis</i>	(179; 1 h)	
(CF ₃) ₂ C=CF ₂	0.76	

Chiefly from refs. 4, 9 and 10, LC₅₀, lethal concentration for 50% of animals, 4 h exposure. ALC, approximate lethal concentration, 4 h exposure.

Little systematic attention has been directed towards determining comparative toxicities, for example LC₅₀ or ALC concentrations, for this type of compound, but we have collected some of the available data in Table 1.

It is clear from descriptions of physiological effects of these olefins that they do not act by a simple physical mechanism but rather by some biochemical interaction. Central nervous system involvement is often observed, particularly when these compounds are examined for possible anaesthesia potential. Further, of the few olefins shown to have high inhalation toxicity and that were also introduced in other ways, the toxicity was high for intravenous injection and also high for oral administration if in lipophilic solutions¹. It seems that there is no reason to expect that olefin hydrolysis is the sole cause of toxicity, although its enhancement of the overall effect can be substantial.

A striking correlation apparently exists between fluoro-olefins and their toxicological properties which has not been previously realized: the toxicity of a halogenated olefin is directly proportional to the reactivity of that olefin to nucleophiles.

We shall not discuss in detail the postulates of nucleophilic substitution at unsaturated fluorocarbons or of fluorocarbon theory. Nevertheless, fluorinated olefins are rather reactive towards nucleophilic reagents to yield mostly substituted products and, more rarely, addition products. One may suggest a carbanion intermediate for these reactions although its descrete existence in some instances is not beyond question. This carbanion concept is useful as a predictor of both reactivity and products⁶. Generally, a fluorine moiety activates a double bond towards nucleophilic attack and the order of reactivity increases with intermediate carbanion stability, that is, 3° > 2° > 1°. For example, we find the following order of nucleophilic susceptibility for perfluorinated olefins:



This ranking is identical to that of the comparative toxicities of these olefins.

Other halogen substituents affect olefin reactivity, usually enhancing it, although there is little information on the comparative kinetics of various fluorinated olefins towards nucleophiles. Most observations of relative nucleophilic susceptibility are deduced from the severity of experimental conditions needed to prepare vinyl ethers by reaction of olefins with alkoxides or alcohols.

In at least one instance, the relative reactivity of a *cis*:*trans* isomer pair was determined. Park and Cook⁷ found that for the reaction of *cis* and *trans*-2,3-dichlorohexafluorobutene-2 with methoxide ion at 25° C, the *trans* isomer was nearly four times as reactive as the *cis* isomer. Raventos and Lemon⁸

have found that the *trans* isomer of this olefin is about three times as toxic as the *cis* isomer.

Surely these are more than coincidental relationships. Alkylating agents—compounds sensitive to nucleophiles—are a well known class of compounds possessing high biological activity⁸. That fluorinated olefins may also be alkylating agents in biological systems must also be considered. Further, it is possible that this is the principal reason for the high toxicity found in many members of this class. Of course, halide hydrolysis is a concurrent toxic mechanism and is doubtlessly responsible for lung oedema and associated disorders. We feel, however, that this hydrolysis is obscuring what is likely to be the principal toxic mode of activity of these compounds. The warning is clear: whenever one works with a poly-fluorinated olefin of high nucleophilic susceptibility, and in the absence of specific toxicological information, extraordinary safety precautions are indicated.

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Chlorinated Hydrocarbon Pesticides and Related Compounds in Adipose Tissue from People of Japan

HERE we report preliminary results on the presence of hexachlorobenzene (HCB) and polychlorinated biphenyls (PCBs) in addition to dichlorodiphenyl trichloroethane (DDT), dieldrin (HEOD), heptachlor epoxide (HE) and the three isomers of hexachlorocyclohexane (α, γ, β -HCCH) in Japanese autopsy adipose tissue. A total of 241 samples were taken at the Aichi Cancer Center Research Institute, Chikusa-Ka Nagoya, Japan.

The fat samples analysed averaged 1.1 g wet weight. The procedure of Mills¹ was essentially followed for extraction and clean-up, and analysis was completed using a Micro Tek MT-220 and a Varian 2100 gas chromatograph equipped with electron capture detectors, ³H or ⁶³Ni. Columns used: (1) 1.5% OV-17/1.95% OF-1 on 'Supelcoport' 80/100 and (2) 5% OV-210 on 'Supelcoport' 80/100, and maintained at temperatures of 200° C and 188° C, respectively. The injection ports were at 250° C, the ³H detector at 200° C, and the ⁶³Ni detector at 315° C. Aliquots of sample extracts were compared qualitatively and quantitatively with a standard chlorinated hydrocarbon mixture (Fig. 1).

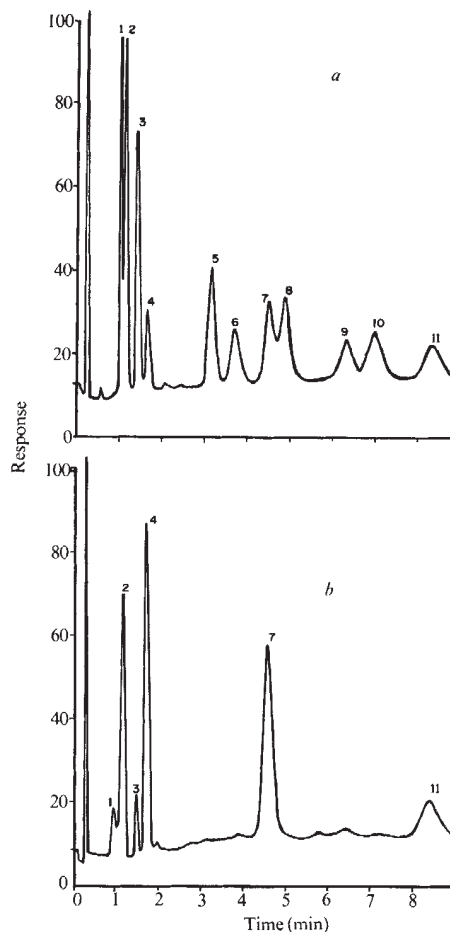


Fig. 1 Gas chromatographic traces of (a), standard chlorinated hydrocarbon mixture; 53 pg each of: 1, hexachlorobenzene; 2, α -HCCH; 3, γ -HCCH; 4, β -HCCH; 5, heptachlor epoxide; 6, *o, p'*-DDE; 7, *p, p'*-DDE; 8, dieldrin; 9, *o, p'*-DDT; 10, *p, p'*-DDD; and 11, *p, p'*-DDT; and (b), Japanese adipose tissue, 0.053 mg. Column, 6 foot $\times$ 1/8 inch glass packed with 1.5% OV-17/1.95% OF-1 on 80/100 'Supelcoport'.

As PCBs have been reported in human tissue^{2,3} it was decided to analyse twenty-five samples at random for possible residue levels of PCBs by electron-capture gas-liquid chromatography following liquid-solid chromatography of the 6% fraction from 'Florisil'. To separate DDT-like materials from the PCBs, twenty samples were analysed by the procedure of Armour and Burke⁴ and five samples by the procedure of Snyder and Reinert⁵. The compound *p, p'*-DDE was not completely resolved as were the other pesticides evident during electron-capture gas-liquid chromatography.

In our experience of residue tissue analysis of polychlorinated biphenyls, stored PCBs elute in the 6% fraction from 'Florisil' and after β -HCCH by gas chromatography on the two columns used in this study. Consequently, pesticide values that would not be questionable because of possible PCB contamination are HCB, α , γ and β -HCCH and dieldrin. To determine the validity of the other pesticide values reported, a comparison of pesticide concentrations before and after separation of PCB was made for the DDT-related compounds and heptachlor epoxide. This was done by comparing the residue levels found in the 6% fraction from 'Florisil' with those found in the second fraction of the PCB-separation procedures.

Two-column gas chromatography, Coulson conductometry and 'Florisil' elution patterns were accepted as sufficient confirmation for the presence of all reported compounds except hexachlorobenzene and PCBs. To substantiate the presence of HCB, one hundred samples were chosen at random and eluted with hexane through Woelm silica gel. After silica gel was

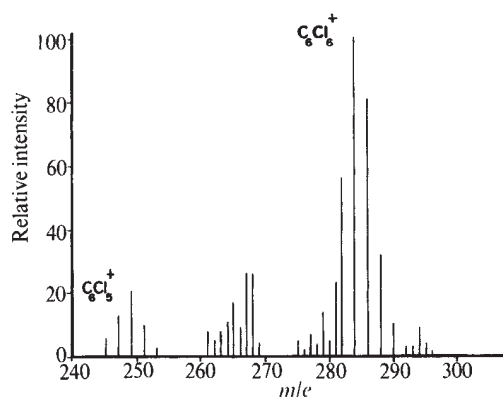


Fig. 2 Partial mass spectrum of hexachlorobenzene in composite Japanese fat. Mass spectroscopy of the composite samples for HCB and PCBs was completed under the following conditions: Instrument, LKB 9000 GC-MS equipped with a mass marker (± 0.3 mass unit); GC column temperature, 209° C; flash heater temperature, 235° C; glass coiled column, 10 foot $\times$ 1/4 inch 1.5% OV-17/1.95% OF-1 on 60/80 mesh 'Chromosorb W', H.P., A.W., DMCS; carrier gas, helium (Prep.); carrier gas pressure, 12 pound inch⁻²; carrier gas flow rate (rotameter setting, 3), 45 cm³min⁻¹; separator temperature, 225° C; source temperature, 290° C; source energy, 70 eV; accelerating voltage, 3.5 kV; trap current, 60 μ A; box current, 50 μ A; and leak current, 8 μ A. (The chlorine isotopic pattern for Cl₂ is slightly distorted due, probably, to impurities.)

deactivated 5% w/v with distilled water, 1.0 g + 0.01 g was added to a 5.75 inch disposable pipette plugged with silanized glass-wool. The column was pre-rinsed with 10 ml. of hexane, and each sample added in a volume of 0.5 ml. It was previously determined that HCB at a concentration of 0.1 p.p.m. eluted quantitatively in 3 ml. hexane.

The eluates were combined, evaporated and analysed by electron-capture and electrolytic conductometric detectors using column 1. Each mode showed three peaks with relative retention times to *p,p'*-DDE of 0.10, 0.19, 0.28 and 0.10, 0.14, 0.22, respectively. Hexachlorobenzene has relative retention times to *p,p'*-DDE of 0.19 and 0.22, respectively.

The composite was pipetted on preparative silica gel (F-254, 2 mm) and codeveloped with an HCB standard for 1 h in a solvent system of petroleum ether, ethyl ether and acetic acid (90+10+1)⁶. Under ultraviolet light (short wave) the quenching of the HCB standard and the composite were observed at an *R_F* of 0.62 and 0.68, respectively. The composite spot was scraped and extracted with hexane, and after evaporation of the extract to 1 ml. the composite and an HCB standard were used to determine and compare *p*-values⁷. The distribution of HCB between equal volumes of hexane and acetonitrile was 0.88 hexane and 0.12 acetonitrile at 25° C. The composite sample had a distribution of 0.86 hexane and 0.14 acetonitrile. These values compare favourably with previously reported data⁸. After *p*-value determination, the composite sample was analysed by mass spectrometry-gas chromatography.

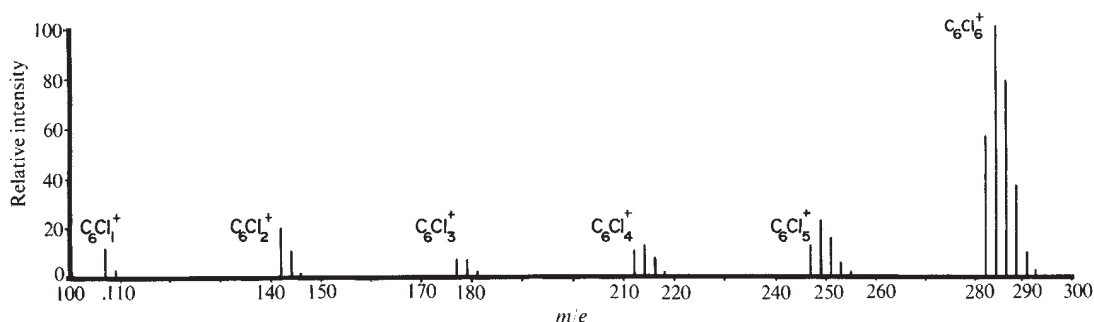


Fig. 3 Mass spectrum of hexachlorobenzene depicting successive loss of chlorine from the parent ion.

Table 1 Concentration of Chlorinated Insecticides in 241 Japanese Fat Samples Measured by Electron-Capture Gas-Liquid Chromatography*

Pesticide	Range	Mean	Standard error ($\pm$)
α -HCCH	<0.003–10.4	0.14	0.04
β -HCCH	<0.007– 8.4	1.28	0.08
γ -HCCH	<0.003– 5.2	0.12	0.02
<i>o,p'</i> -DDE	<0.01 – 0.29	0.03	0.002
<i>p,p'</i> -DDE	<0.01 –16.5	1.78	0.13
<i>o,p'</i> -DDT	<0.01 – 1.12	0.08	0.006
<i>p,p'</i> -DDT	<0.01 – 3.09	0.54	0.03
<i>p,p'</i> -DDD	<0.01 – 0.58	0.04	0.004
HE	<0.01 – 0.2	0.02	0.002
HEOD	<0.01 – 0.98	0.13	0.01
HCB	<0.003– 0.77	0.08	0.006

* In p.p.m.

As the apparent presence of PCB would affect the pesticide levels, it was felt that their presence should be confirmed. A composite sample of PCB fractions was analysed by electrolytic conductivity. It was found that *p,p'*-DDE was not completely resolved from PCB. Following gas chromatography the composite sample was streaked on preparative silica gel (F-254, 2 mm) and codeveloped for 1 h with 'Aroclor 1254' in hexane: methylene chloride, 80 : 20 (ref. 9). 'Aroclor 1254' has an *R_F* value of 0.38. A corresponding area of the sample was scraped, extracted, streaked again on preparative silica gel and codeveloped in the solvent system: petroleum ether, diethyl ether and acetic acid (90+10+1) with 'Aroclor 1254' for 1 h. In this system 'Aroclor 1254' had an *R_F* of 0.52 and the composite was 0.57. The composite spot was scraped, extracted with hexane and analysed by gas chromatography-mass spectrometry.

The initial data resulting from the usual method for the determination of chlorinated hydrocarbons are summarized in Table 1. The levels of the more common chlorinated hydrocarbons, DDT, dieldrin and heptachlor epoxide were within the range found in the United States¹⁰. The levels for three of the hexachlorocyclohexane isomers were quite high, particularly β -HCCH, when compared to American levels¹⁰. Japanese researchers^{11,12} have found generally high levels of the hexachlorocyclohexanes in food and water which could explain the high levels found in the human samples. Traces of the fungicide hexachlorobenzene were also detected.

All samples analysed were positive for PCBs (Table 2). Eighty per cent of the samples had a PCB concentration of less than 1.0 p.p.m.

A comparison of pesticide concentrations, before and after the separation of PCBs for the DDT-like materials, shows that the average percentage of the initial GC response confirmed to be pesticide was HE (62), *o,p'*-DDE (71), *p,p'*-DDE (83), *o,p'*-DDT (50), *p,p'*-DDD (64), and *p,p'*-DDT (85). It seems, for this small sample group, that when PCBs are present they influence the pesticide values of *o,p'*-DDT, HE, *p,p'*-DDD, *o,p'*-DDE more so than *p,p'*-DDE and *p,p'*-DDT.

The normalized mass spectrum of the composite sample

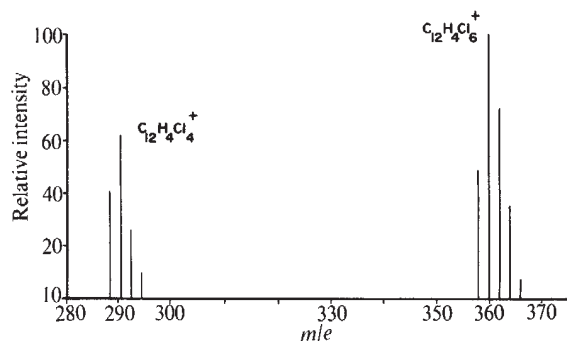


Fig. 4 Partial mass spectrum of hexachlorobiphenyl (PCB) in composite Japanese fat.

analysed for HCB is shown in Fig. 2. The mass spectrum indicates a molecular ion at $m/e=282$. A chlorine isotopic cluster of six chlorine atoms was observed and indicated that an empirical formula for this ion cluster would be $C_{12}H_4Cl_6$. Further examination of the mass spectrum reveals only one major fragment at $m/e=247$, containing a chlorine isotopic cluster of five chlorine atoms indicating the loss of one Cl atom from the parent ion.

Mass spectral examination of an HCB standard (Fig. 3) shows the molecular ion at $m/e=282$ and fragments at $m/e=247$, 212, 177, 142 and 107 with isotopic clusters indicative of five, four, three, two and one chlorine atoms, respectively. The absence of the ion fragments in the low mass range of the spectrum of the composite sample resulted from, first, a low sample enrichment in the analyser tube; and second, the presence of more abundant ions contributed by compounds of high carbon content, similar to fats.

The spectrum contains the expected substituted benzene fragmentation pattern. The parent ion and subsequent ion fragment support the gas chromatography, liquid-solid chromatography, thin layer chromatography and p -value data indicating the presence of HCB in the composite samples. The normalized mass spectrum of the composite sample analysed for hexachlorobiphenyl is shown in Fig. 4. This composite sample was found to contain p,p' -DDE, which was evident at an earlier stage of analysis. Although earlier analysis showed the presence of several PCB-type constituents, only one was of sufficient concentration for mass spectral confirmation. The molecular ion at $m/e=358$ with a chlorine isotopic cluster of 6 is the hexachlorobiphenyl with a fragment at $m/e=288$ containing four chlorine atoms. The loss of chlorine atoms in pairs from the parent ion has been the PCB fragmentation pattern observed in this laboratory.

The presence of a fungicide HCB, a chlorinated biphenyl and normally occurring pesticides has been confirmed in human adipose tissue from Japan. The contribution that the presence of PCB has on the reported storage values of the more commonly occurring pesticides has been shown. The levels of HCHs, PCBs and DDT are slightly lower but of the same

order of magnitude as those reported by Nishimoto *et al.*¹³. HCB was not reported by these workers.

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Use of "Whole Egg Residues" in Pesticide/Eggshell Studies

HAZELTINE¹ questions the well established belief that DDE probably causes eggshell thinning in brown pelicans chiefly by finding four points of disagreement with the proposal by Blus *et al.*² that a concentration-effect relationship seems to exist between DDE in eggs and shell thickness. In their subsequent reply, Blus *et al.*³ refute Hazeltine's criticisms. There is a further argument against Hazeltine's third criticism of Blus *et al.*'s conclusions; and the argument has an important bearing on the interpretation of analyses based on "whole egg residues".

Hazeltine expresses the view that the "whole egg residues" are valueless in pesticide/eggshell studies of incubated eggs on the basis of his assumption that the residues are metabolized during incubation. He provides no data for residues expressed on a whole egg (fresh weight) basis, and gives no acceptable evidence to show that DDE or other residues are metabolized (that is, broken down chemically), as distinct from mobilized. Even if we accept that the residues are indeed metabolized during incubation, this does not necessarily make the use of the whole egg residues inappropriate. If DDE residues are metabolized during incubation, then the whole egg residues for incubated eggs will tend to be low. Bearing in mind the thinning of eggshells by withdrawal of calcium in embryonic development during incubation, it is obvious that in the presence of DDE metabolism during incubation, the use of the whole egg

Table 2 Concentration of Polychlorinated Biphenyls in Japanese Fat *

Number of samples analysed	Range	Mean§	Standard error (±)
5 †	0.45–0.56	0.51	±0.017
20 ‡	0.30–1.48	0.80	±0.065

* In p.p.m.

† PCBs separated by method of Snyder and Reinert, AR 1254 at 0.5 p.p.m. gave 62% recovery in fraction I ($N=3$).

‡ PCBs separated by method of Armour and Burke, AR 1254 at 0.5 p.p.m. gave 87% recovery in fraction I ($N=3$).

§ These values are based on total area under the curve using 'Aroclor 1254' as a reference standard and are exclusive of sample responses with the same retention time as p,p' -DDE, no correction was made for standard recovery.

residues for pesticide/eggshell studies would provide a conservative test if the correlation between the eggshell thickness and the levels of residue is asserted to be negative. Blus *et al.*'s "highly significant regression ($P < 0.01$)" with a negative slope is then likely to be even more significant than suggested by the probability value quoted.

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³ Blus, L. J., Gish, C. D., Belisle, A. A., and Prouty, R. M., *Nature*, **240**, 164 (1972).

DDE in Eggs and Embryos of Brown Pelicans

HAZELTINE¹ claims to have demonstrated that DDE residues are metabolized by developing embryos of brown pelicans (*Pelecanus occidentalis*). This conflicts with experimental work² on Japanese quail (*Coturnix coturnix*), in which incubation did not seem to affect total residue levels in eggs, except for some conversion of *p,p'*-DDT to *p,p'*-DDE.

Hazeltine's claim seems to be based on a comparison of DDE levels in the yolks of four incubated and five fresh eggs. As he made clear in the text, the column labelled "Weight yolk" in his Table 1 actually refers to the yolk plus embryo. The apparent 3.2-fold decrease in the mean concentration of DDE in "yolk" simply reflects the 2.6-fold increase in the weight of the yolk+embryo, as the embryos absorbed material from the white. In Hazeltine's sample the whole-egg residues of DDE were slightly smaller in the incubated eggs (mean 2.53 mg) than in the fresh eggs (3.62 mg), but the difference is not statistically significant and in any case this does not demonstrate metabolism of DDE. It is more simply explained by the fact that eggs with higher levels of DDE are broken more frequently during incubation, so that they are less frequently available for collection: this differential breakage has been demonstrated not only in the brown pelican³, but also in other species⁴⁻⁷. For the same reason³⁻⁷ samples of incubated eggs are expected to have thicker shells, on the average, than fresh eggs, as in Hazeltine's sample (means 0.390 mm and 0.372 mm, respectively).

Hazeltine also reported that eggshell thickness was positively correlated with DDE concentration in the lipids of the "yolk". But the latter is not an appropriate measure of the DDE levels in the eggs, because it increases during incubation as the egg lipids are reduced by metabolism⁸ (from 3.80 g to 2.26 g in Hazeltine's sample). The most appropriate measures are the whole-egg residue or whole-egg concentration, which reflect the levels of DDE circulating in the female at the time of laying⁹⁻¹¹. In Hazeltine's sample, the Spearman rank correlation coefficient r_s between whole-egg residue of DDE and eggshell thickness is +0.244 (not +0.477 as stated in Hazeltine's Table 2). This is not statistically significant, which is not surprising in a small sample with a very small range in eggshell thickness: but the points fall close to the regression lines of Risebrough¹² and Blus *et al.*¹³. As Hazeltine points out (his Table 3), in Risebrough's larger sample the correlation is negative and highly significant ($r_s = -0.4318$, $P < 0.01$).

Hazeltine also stated that non-parametric statistics should have been used by Blus *et al.*¹³ to test the relationship between eggshell thickness and DDE residues, because these variables were "not bi-variantly normally distributed". This would be valid if the goal of the study had been simply to demonstrate

association of eggshell thinning with DDE, but Blus *et al.*¹³ were attempting to define the dose-response relation. Parametric regression techniques require only that the dependent variable be random and normally distributed about the regression line¹⁴. This condition was satisfied by the brown pelican eggshell data of both Risebrough¹² and Blus *et al.*¹³, and both found a good fit to a logarithmic dose-response relation. A logarithmic relation between eggshell thickness and DDE residues in eggs has also been reported in wild peregrine falcons (*Falco peregrinus*)^{4,15} and in experimental mallards (*Anas platyrhynchos*)¹⁶. The advantage of applying a logarithmic transformation to the DDE variable is that it is then possible to use multiple linear regression techniques to separate the effects of co-existing pollutants. This was done by both Blus *et al.*^{17,18} and Risebrough¹², who found independently that most of the variance in eggshell thickness was explained by the log DDE and DDE variables, and no significant fraction by any other chemicals.

Hazeltine also criticized Blus *et al.* for combining data from brown pelicans of two different subspecies. Blus *et al.* corrected for the known difference between the subspecies by using as dependent variable the eggshell thickness expressed as a percentage of the pre-1947 mean for the subspecies. In any case this criticism cannot be applied to Risebrough's data, which were all drawn from Pacific Coast populations¹².

The association of eggshell thinning in birds with *p,p'*-DDE is one of the best known of all environmental phenomena¹⁹. It has been shown so many times in both wild and captive species^{3-7,12,13,16-18} that at least one journal has complained about receiving further "verifications of phenomena already fully demonstrated"²⁰. Scientific work in this area is now devoted to elucidating details such as the form of the dose-response relation and the reasons for the known interspecific differences in sensitivity. The brown pelican is one of the species in which the phenomenon has been explored most fully^{9,12,13,17,18,21,22}. It is therefore somewhat odd to find another letter¹ discussing whether the association exists, based on a sample too small and homogeneous to demonstrate anything. In fact, Hazeltine's nine eggs fall exactly into the pattern of eggshell thinning known from previous work^{12,13,22}, and his data add nothing to previous knowledge except for his demonstration that "yolks" grow larger during incubation.

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Inhibition of Lectins by Antifreeze Glycoproteins from an Antarctic Fish

CERTAIN Antarctic fishes can resist freezing, even at ambient water temperatures as low as -1.9°C , partly because of the presence in their serum of a unique group of "antifreeze" glycoproteins¹⁻⁵. These glycoproteins are composed of repeating units of the triglycopeptide, Ala-Ala-Thr-O-disaccharide. The disaccharide is galactosyl-N-acetylgalactosamine, with internal linkage β , 1 $\rightarrow$ 3 (ref. 6) or β , 1 $\rightarrow$ 4 (ref. 7). Three active glycoproteins differing only in polymer length have been characterized with molecular weights of approximately 11,000, 17,000, and 22,000. In addition to these active glycoproteins, two smaller related glycoproteins have been found. These differ from the large active glycoproteins by their comparative inactivity in depressing the freezing point, their smaller molecular weights (approximately 2,500 and 4,500), and the substitution of a proline for some of the alanines following threonine^{8,9}.

We initiated immunological studies in an attempt to develop sensitive methods for studying these glycoproteins. Both the active and inactive glycoproteins failed to precipitate with horse antipneumococcal type IV or type XIV sera (unpublished observations of M. J. Heidelberger, jun.). At Heidelberger's suggestion we made tests for inhibition of the haemagglutination by plant lectins. In this way we have demonstrated a distinct difference between these active and inactive antifreeze fish glycoproteins.

The active and inactive antifreeze glycoproteins were prepared from the blood serum of specimens of the fish *Trematomus borchgrevinki*, caught in Antarctica. The blood was centrifuged after it had clotted; the clear serum was frozen for transport to the University of California, Davis. Purification of the active and inactive antifreeze glycoproteins was as previously described¹. The active antifreeze was a mixture of fractions one to five and the inactive fractions were mixtures of seven and eight¹.

Lectins were prepared from slurries of finely ground seeds made up (20% w/v) in 0.15 M NaCl, extracted overnight at 4°C and cleared of insoluble materials by coarse filtration through surgical gauze and centrifugation at 10,000g for 10 min. Considerable inactive coagulum was removed by subjecting the clarified extracts to 65°C for 20 min followed by recentrifugation. Sodium azide (0.1%) was added as a preservative and the lectin preparations were then stored at 4°C without notable loss of activity.

To study the effects of holding live *T. borchgrevinki* at a temperature above the freezing point, approximately 30 fish were placed in temperature-controlled tanks in the bio-laboratory at McMurdo Station, Antarctica. The temperature of these tanks was maintained at $3 \pm 1^{\circ}\text{C}$. Fish were taken and bled at weekly intervals until termination of the experiment at 5 weeks. The blood was handled as above.

Samples of mammalian saliva from both "secretor" and "non-secretor" individuals were prepared as previously described¹⁰. All sugars were of reagent grade; α - and β -lactose preparations were provided by J. R. Spies.

Small molecular weight glycopeptides were prepared from active antifreeze as previously described³. Mixtures of small glycopeptides (mainly di- to hexa-glycopeptides) were separated from the digest by electrophoresis.

Other samples of blood plasma or serum were obtained by centrifugation of the clotted or unclotted blood from human donors in the laboratory, from salmon (*Oncorhynchus tshawytscha*) (obtained from the California Fish and Game Division) or from rabbits (obtained from the animal colony at Davis). Blood cells of diverse origin were available from regular laboratory stocks or from the School of Veterinary Medicine at Davis. Haemagglutination tests and sugar inhibition studies were carried out as previously described^{10,11}.

In Table 1 we show the potency with which the antifreeze-active glycoprotein inhibited haemagglutination by Osage-orange (*Maclura pomifera*) lectin. At a final concentration in the reaction mixtures of less than $1\text{ }\mu\text{g ml}^{-1}$ the active antifreeze glycoprotein completely inhibited haemagglutination of both human group-O and sheep erythrocytes. By contrast, the inactive antifreeze glycoprotein was some fifty to one hundred times less active as an inhibitor. Several other randomly tested preparations containing glycoproteins of diverse origin were either inactive or comparatively weak inhibitors (Table 1).

The active antifreeze and inactive antifreeze glycoproteins tested at $100\text{ }\mu\text{g ml}^{-1}$ starting concentration also failed to inhibit numerous other lectins as well as immune animal sera possessing various haemagglutinating specificities. The striking inhibitory activity of the intact active antifreeze glycoprotein for the Osage-orange lectin was further illustrated by the finding of little or no inhibitory activities by either the blood sera of man, rabbit, and a cool-water fish, the salmon; or preparations of

Table 1 Haemagglutination Inhibitors

Agglutinating reagent	Erythrocytes tested	1:8-titre agglutinating reagent mixed with equal volume of:							Antifreeze glycoprotein†	
		Saliva*		Rhesus Sec	Serum		Ovomucoid‡		Active	Inactive
		Human Non-sec	O sec		Fraction VI†	Sheep				
Osage-orange lectin	Human O	(2)	(16)	(64)	(32)	(4)	+++		(800)	(8)
	Rhesus	(1)	(2)	(64)	(4)	(1)	+++		(200)	(4)
	Sheep	++	(8)	(64)	(64)	(4)	+++		(600)	(8)
Ricin	Human O	++	++	(2)	(1)	+++	++	++	++	++
	Rhesus	++	++	(4)	(4)	+++	++	+++	+++	+++
	Chicken	++	+++	(4)	(2)	++	+++	+++	+++	+++

* Sec=boiled "secretor" saliva.

† Commercial glycoprotein preparations tested as inhibitors at a starting concentration of 1 mg ml^{-1} .

‡ Tested at starting concentrations of 1 mg ml^{-1} .

Numbers enclosed by parentheses denote reciprocal of maximum dilution of inhibitor solution which still completely inhibited macroscopic agglutination when mixed with an equal volume of 1:8-titre agglutinating reagent before the introduction of one volume of a 2% suspension of thrice saline-washed erythrocytes. Non-inhibited macroscopic agglutination graded from + to +++ following 20 to 30 min tube incubation at 22° and centrifugation for 15 s at 1,000g.

mixtures of small glycopeptides produced by elastase hydrolysis of active antifreeze glycoprotein. Also, when live specimens of *T. borchgrevinki* were kept at $3 \pm 1^\circ \text{C}$ for periods of up to five weeks, the lectin-inhibition titres did not change. The antifreeze activities of the blood also did not appear to change significantly during this time, although fluctuations were noted.

In comparative studies of inhibition with 11 different monosaccharides, three sugars with D-galactose configuration (N-acetylgalactosamine, D-galactose, and 2-deoxy-D-galactose) and α -methyl-D-mannoside notably inhibited the Osage-orange lectin, decreasing in potency in the order indicated. No detectable inhibition was obtained with 6-deoxy-D-galactose (D-fucose), L-fucose, D-glucose, D-mannose, or 3-O-methyl-D-glucose tested at 0.5 M starting concentration.

Of four oligosaccharides with non-reducing end-groups of D-galactose (tested at a 10% (w/v) starting concentration), only melibiose and raffinose notably inhibited the Osage-orange lectin. α - and β -Lactose were both ineffectual inhibitors of the Osage-orange lectin, notwithstanding the internal β linkage in the antifreeze disaccharide moieties. Our observations, nevertheless, are largely consistent with earlier and more extensive oligosaccharide inhibition studies on the Osage-orange lectin¹²⁻¹⁴. In one of these¹⁴ a disaccharide with a reported structure possibly identical with the antifreeze disaccharide (β -D-galactosyl-N-acetylgalactosamine) was less active as an inhibitor of the Osage-orange lectin than either melibiose (α -D-galactosyl-(1 $\rightarrow$ 6)-D-glucose) or N-acetylgalactosamine.

Notable inhibition of the Osage-orange lectin by D-galactose, N-acetylgalactosamine and 2-deoxy-D-galactose, but not by 6-deoxy-D-galactose, in turn indicates the likely participation in Osage-orange lectin interactions of hydroxyl groups at the 3, 4, and 6 carbon positions of the terminal D-galactosyl residues in the intact antifreeze-active glycoprotein. None of the *T. borchgrevinki* glycoproteins inhibited the castor-bean lectin (Ricin), which is inhibitable with either D-galactose or 6-deoxy-D-galactose and is reportedly reactive with all D-galactosyl residues possessing accessible hydroxyl groups at the 2, 3, and 4 carbon positions¹⁵. These observations indicate strongly that the hydroxyl groups at the 3, 4, and 6 carbon positions of the terminal D-galactosyl residues of the intact active antifreeze glycoproteins are important for the interaction with Osage-orange lectin. It seems that the polypeptide backbone or adjacent disaccharides in the repeating triglycopeptide units confer on the terminal D-galactosyl residues in the intact active antifreeze glycoprotein molecules a spatial positioning particularly favourable for interactions with the Osage-orange lectin. The only other possibility seems to be the existence of an unrecognized structure which is hydrolysed by the elastase.

The quantities of freezing-point depressing glycoproteins required for the inhibition of the lectin and depression of the freezing point are $<0.1 \mu\text{g}$ and $>1.0 \text{ mg}$, respectively; that is, the lectin assay is $>10^4$ times more sensitive. The lectin assay therefore provides a micro method for determining the amounts of the glycoprotein in tissues and fluids of polar fishes and for studying its biosynthesis and metabolism.

Both the activity for inhibiting the lectin and the activity for depressing the freezing point seem to be dependent upon the primary structure of the glycoproteins with regular spacings of the disaccharides along the peptide chain. This has been shown for both processes by the very low activities of the glycopeptides obtained by proteolysis from the active freezing point-depressing glycoproteins and the very low activity of the smaller molecular weight inactive freezing point-depressing glycoproteins. Other studies have shown that oxidation of C-6 alcohol groups of the galactose residues to carboxyl groups destroys activity for inhibiting the lectin as well as for depressing the freezing point^{6,7}. Further studies on relating structural requirements for these two different activities are under way¹⁶.

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Are Mosquitoes Monogamous?

CONFUSION has arisen within the past 5 years with regard to two related aspects of the most basic feature of the sexual behaviour of mosquitoes. The first aspect concerns the definition and use of the word, *monogamous*. In various studies on the biology of reproduction in mosquitoes, Craig and his associates¹⁻³ refer to "monogamous" female mosquitoes using it to refer to one sex exclusive of the other, as if the term were derived from the word gamete and could be used to refer to a female mosquito that had received the spermatozoa from only one male. The word monogamous is in fact derived from a Greek word γαμος (gamos) meaning marriage⁴, and, since 1758 the zoological definition has been "the habit of living in pairs, or having only one mate"⁴. The word gamete, on the other hand, is derived from a Greek word γαμετη (gameta), meaning either husband or wife⁴. The word mate is defined as an associate or companion, or one of a pair of animals. Both the Greeks and the English have separate words for sex, copulation and insemination, and a totally different word

monogamous for having only one mate. The word monogamous is complicated because it can mean having only one mate at a time or having only one mate for life. Having one mate does not necessarily mean that the individuals of one pair copulate; the word copulate means to join, couple, unite, or connect but does not specify insemination. It will be shown in the following section that Craig's use¹ of the word monogamous is peculiarly inappropriate for the mosquito *Aedes (Stegomyia) aegypti* (L.).

The second aspect of this problem concerns a seemingly simple direct observation of whether an individual female *A. aegypti* copulates more than once during her lifetime. It was originally believed that *A. aegypti* females copulate with many males under free-flying conditions in the laboratory⁸. Roth⁵ observed that one male in a cage with 16 virgin females copulated 30 times in 30 min, and that 11 males copulated 50 times in 1 h with a single previously virgin female. Wheeler and Jones⁶ found that male *aegypti* could be forced to copulate with some newly-emerged females but did not inseminate them. This was influenced by the secretions of the corpora allata and varied with the strain of *aegypti*⁷. Male *aegypti* could not be force-copulated with freshly inseminated females⁸. While under free-flying conditions many of the once-mated females copulated a second, although significantly shorter, time than the first⁹. While Gwadz and Craig² stated that *aegypti* females may copulate repeatedly, it was subsequently concluded, from observations with tethered females³, that they copulate only once and falsely seem to copulate thereafter. Gillett¹⁰ reported many individual and sequential (single pair) matings of *aegypti*, and that one free-flying female mated with 40 different males.

My observations were made on the Bangkok strain of *A. aegypti*. To demonstrate whether free-flying females would copulate (or seem to copulate) with only one male and with this male more than once, ten individual couples were placed in separate cages and observed under undisturbed conditions 4 h per day for 5 to 7 days. Most of the couples copulated (or seemed to do so) more than once with a given partner under these strictly monogamous conditions. The maximum number of copulations occurred on the third day of monogamous cohabitation, when the caged mosquitoes flew about more often than on other days. Over a 7-day period, four out of five couples made 75 genital contacts during 28 h of direct observation; one couple was never seen to copulate. I conclude that females will copulate repeatedly with the same male when only one is available. Females in cages with many males have also been seen to couple repeatedly with one male.

It was possible in many cases to distinguish clearly between pseudocopulations and true copulations among free-flying mosquitoes in a cage. Most pseudocopulations were very short contacts (less than 1–4 s); the males either attached their claspers to a female's cerci or else clasped her terminal sternum and in either case only lightly. Often the males made a series of rapid thrusts with their terminalia in the direction of the female's terminalium without actually clasping any structures of the female.

To determine whether females would copulate with more than one male, a female which had had 13 observed genital contacts with one male over a 6-day period was sequentially placed in a series of 5 cages, each with a different virgin male, and the cages were manually agitated periodically for 5 min to induce flight activity. While only pseudocopulations were seen with each of the first 4 males, the fifth male definitely copulated with this female and for an abnormally long time (250.7 s). After this, a series of virgin females of known ages (1 to 13 days old) were individually blown into a cage of 20 highly active males and observed for 5 min. The 52 females were continuously disturbed to fly whenever they landed, and appeared to copulate with from 1 to 12 males in 5 min with an average of about 5 males. During these tests, 2 males, were seen attempting to copulate simultaneously with one female in 14 cases, 3 males were observed trying to establish genital contact with one female at the same time in 9 cases, and more than 3

males were found trying to mate with a single female concurrently on 4 occasions. Similar activities can be observed in colony cages. In a special test, one female was observed to copulate (or pseudocopulate) with a total of 15 different males over a period of 3 days.

The duration of the first genital contact versus the longest subsequent contact was recorded for 47 couples during these studies. It was found that in 57.4% of the cases, the longest copulation was not the first one. In general, the second genital contact (when it occurred shortly after the first copulation) was significantly shorter than the first one and was often a pseudocopulation.

When virgin females were placed in cages with 5 virgin males and the cages manually shaken for 5 min, first copulations almost invariably resulted in insemination, if the individuals remained in genital contact for 6 s. It was necessary to use only virgin males in these tests because it was found that when 43 virgin females were individually blown into a cage containing 20 unchanged males, only 74% were inseminated by the first copulation.

I conclude that while *Aedes aegypti* may copulate repeatedly with only one mate over a period of days under strictly monogamous conditions, under normal laboratory conditions this species is a polygamous insect, and that the female normally copulates more than once with one or many males but usually gets inseminated only once if she is a virgin when she copulates. This is in agreement with the earlier work of Roth⁵ and Gillett¹⁰, but not with Gwadz *et al.*², that the female of this species copulates only once during her lifetime.

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Competitive Exclusion in Herbaceous Vegetation

In maintaining or reconstructing types of herbaceous vegetation in which the density of flowering plants exceeds 20 species/m²—the so-called "species-rich" communities, success is often frustrated by competitive exclusion. Here I describe an attempt to identify criteria with which to assess or anticipate the effect of competitive exclusion both at individual sites and in different types of vegetation.

Herbaceous plants have been classified according to the extent to which certain competitive attributes are evident in the genotype. Four consistent features of "competitive" species may be recognized^{1–14}. They are (1) tall stature; (2) a growth form (usually a large densely-branched rhizome or expanded tussock structure) which allows extensive and intensive exploitation of the environment above and below ground; (3) a high maximum potential relative growth rate,

Table 1 Examples illustrating the Derivation of the Competitive Index

Species	Attributes				Competitive index (total/2)
	a	b	c	d	
<i>Chamaenerion angustifolium</i>	5	5	5	2	8.5
<i>Arrhenatherum elatius</i>	5	4	4	3	8.0
<i>Brachypodium pinnatum</i>	3	4	3	5	7.5
<i>Ranunculus repens</i>	3	5	3	1	6.0
<i>Helictotrichon pratense</i>	3	2	3	2	5.0
<i>Taraxacum officinale</i>	3	1	4	1	4.5
<i>Festuca ovina</i>	2	1	3	2	4.0
<i>Campanula rotundifolia</i>	2	2	3	0	3.5
<i>Arenaria serpyllifolia</i>	1	0	4	0	2.5

a, Maximum plant height (Clapham, Tutin and Warburg¹⁵). 1, <26 cm; 2, 26–50 cm; 3, 51–75 cm; 4, 76–100 cm; 5, >100 cm. b, Morphology (Clapham, Tutin and Warburg and personal observations). 0, Small therophytes; 1, robust therophytes; 2, perennials with compact unbranched rhizome or forming small (<10 cm diameter) tussock; 3, perennials with rhizomatous system or tussock attaining diameter 10–25 cm; 4, perennials attaining diameter 26–100 cm; 5, perennials attaining diameter >100 cm. c, Maximum potential relative growth rate (Grime and Hunt, unpublished). 1, $RGR_{max} < 2.1 \text{ mg g}^{-1} \text{ h}^{-1}$; 2, $2.1\text{--}4.0 \text{ mg g}^{-1} \text{ h}^{-1}$; 3, $4.1\text{--}6.0 \text{ mg g}^{-1} \text{ h}^{-1}$; 4, $6.1\text{--}8.0 \text{ mg g}^{-1} \text{ h}^{-1}$; 5, $>8.0 \text{ mg g}^{-1} \text{ h}^{-1}$. Where no estimate is available a provisional score of 3 has been used. d, Maximum accumulation of persistent (from one growing season to the next) litter produced by the species (personal observations). 0, None; 1, thin discontinuous cover; 2, thin continuous cover; 3, up to 1 cm depth; 4, up to 5 cm depth; 5, >5 cm depth.

and (4) a tendency to deposit a dense layer of litter on the ground surface. It is practicable to score plant species with respect to each of these features and to use the sum of the scores to provide a competitive index (CI) over a scale of 0–10 (Table 1).

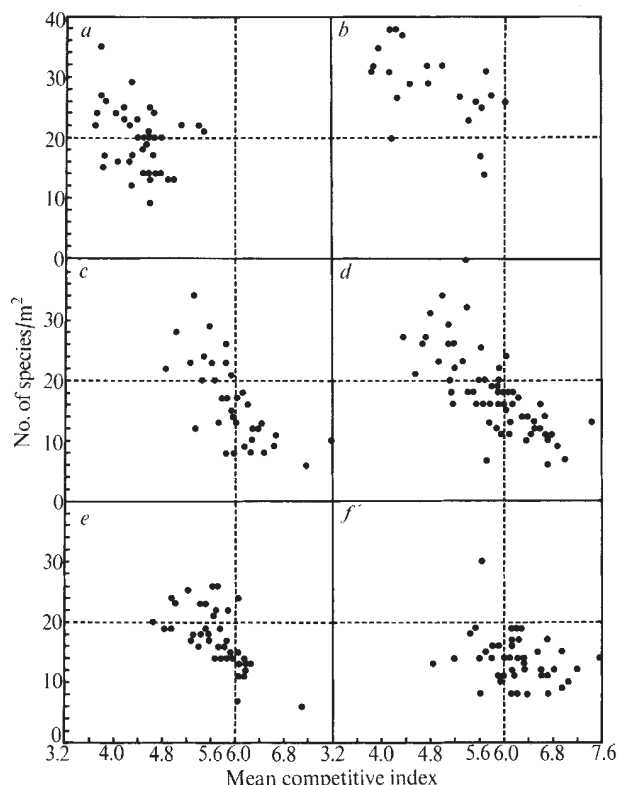


Fig. 1 Relationship between “mean competitive index” and species density in six habitats sampled widely from the same geographical area (Grime and Hodgson, unpublished). a, Limestone outcrops with discontinuous soil cover; b, unenclosed limestone pastures; c, enclosed pastures; d, derelict limestone grassland; e, meadows; f, road verges. The contribution of each species to the mean competitive index is weighted in proportion to its frequency in the m^2 sample of vegetation.

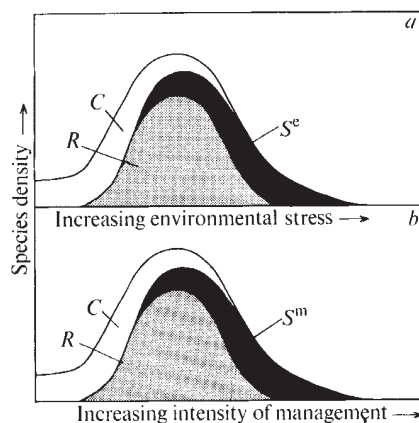


Fig. 2 Diagrams representing impact upon species density of (a) intensity of environmental stress and (b) intensity of grazing, mowing, etc. C, Species of high competitive index. S^e , S^m , S^b , S^t , Species (or ecotypes) of high resistance to the prevailing stresses imposed by environment or by grazing, mowing, burning or trampling respectively. R, Remaining species.

As it has been calculated in this paper, the CI incorporates a subjective component, fails to take account of ecotypic variation and ignores certain competitive attributes such as the release of phytotoxic compounds. Despite this lack of refinement, however, the index appears to be informative.

In Fig. 1 the CI has been used to assess the importance of competitive exclusion in the control of species density in six types of vegetation sampled from the same geographical area. For each square metre sample of vegetation a mean value calculated from the competitive indices of the component species has been plotted against species density. The data confirm that where species of high CI are prominent (that is mean $CI > 6.0$) species densities are consistently low ($<20 \text{ species m}^{-2}$). The results indicate a low incidence of competitive exclusion on limestone outcrops and in limestone pastures. In contrast, there is strong evidence that competition is a causal factor in the maintenance of the rather low species densities encountered in the samples from road verges. In the three remaining types (enclosed pastures, derelict limestone grassland and meadows) species density varies widely but in each there is a marked decline with increasing mean CI.

On the basis of previous studies^{7,11,14,16–20} and the results of this investigation, I suggest that two mechanisms may bring about the low incidence of species of high CI in vegetation of high species density. One is the result of environmental stress induced by factors such as drought and mineral nutrient deficiencies, and the other is brought about by phenomena such as grazing, mowing, burning and trampling, which by defoliation or by causing other forms of damage to the vegetation tend to prevent potentially competitive species from attaining maximum size and vigour and reduce litter accumulation.

A parallel exists, therefore, between the influence of increasing environmental stress and that of increasing damage intensity, by grazing or mowing for example, on species density. According to the model proposed in Fig. 2a, under conditions of low environmental stress productivity is high and species of high CI attain maximum vigour and species density is low owing to competitive exclusion. Under conditions of increased environmental stress, the competitive species decline in vigour and species of lower competitive ability are able to survive. With further reductions in productivity species density falls as conditions of extreme environmental stress are reached and species density is limited by the scarcity of species tolerant of the specific conditions limiting productivity. This model is consistent with the observation of Odum³⁰ that “the greatest diversity occurs in the moderate or middle range of a physical

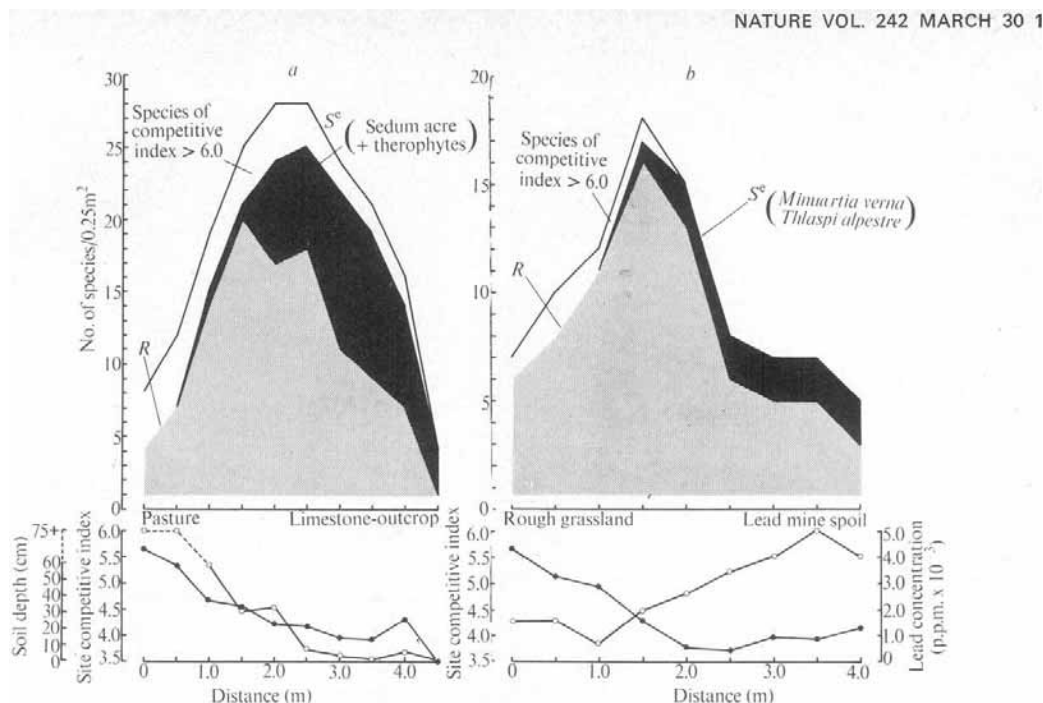


Fig. 3 Transects along natural gradients of increasing environmental stress. *a*, Boundary between rough pasture and a limestone outcrop (Coombsdale, Derbyshire). *b*, Margin of a spoil heap at a derelict lead mine (Winster, Derbyshire). Lead was extracted from the surface soil (0–3 cm) using normal ammonium acetate adjusted to pH 3.0. Shading and symbols as in Fig. 2.

gradient." Data conforming to the model have been obtained from transects along naturally-occurring gradients in environmental stress (Fig. 3).

With respect to the gradient of increasing intensity of grazing, mowing, etc. (Fig. 2*b*), the pattern is essentially similar. Assuming that productivity is sufficiently high, competitive exclusion will occur at low intensity of defoliation and damage. At higher intensities, species of high CI are suppressed and conditions favourable to less aggressive species occur. At the highest intensities species density would be expected to fall as a situation is reached in which only a small number of species are tolerant of the specific form of damage sustained. It is difficult to find situations in the field which illustrate all features of the latter model. Gradients in intensity of factors such as grazing, mowing and burning rarely extend over the full range represented in Fig. 2*b*. A possible exception to this arises in conditions of excessive trampling (Fig. 4) although here it is recognized that effects such as soil compaction may be involved, causing environmental stress.

From a practical standpoint, therefore, there is a need to determine the relative importance of such extrinsic factors in maintaining high species density at particular sites. A possible solution to this problem is to recognize the inverse relationship between net environmental stress and productivity and to use the maximum potential relative growth rates (RGR_{max}) of the perennial species present at each site to derive an index of the latter. A correlation between RGR_{max} and site productivity may be inferred from a number of studies^{19,31–34} and comparisons such as that illustrated in Fig. 5 confirm that there is a consistent difference between productive and unproductive vegetation with respect to the potential growth rates of the component perennial species.

An index based upon RGR_{max} would appear to be promising not only in field assessments of the intensity of grazing, mowing, burning or trampling necessary to initiate or maintain high species density but also as a guide to the

stability of herbaceous vegetation. It is to be expected that vegetation composed of species with high potential growth rates (especially where some are suppressed specimens of species of High CI (Fig. 5*a*)) will show a rapid decline in

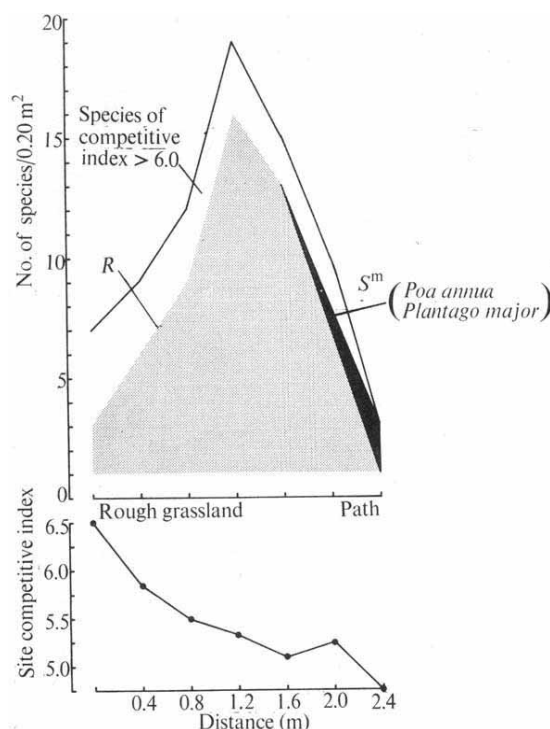


Fig. 4 Transect across the margin of a path through rough grassland (Maltby Low Common Nature Reserve, Yorkshire). Shading and symbols as in Fig. 2.

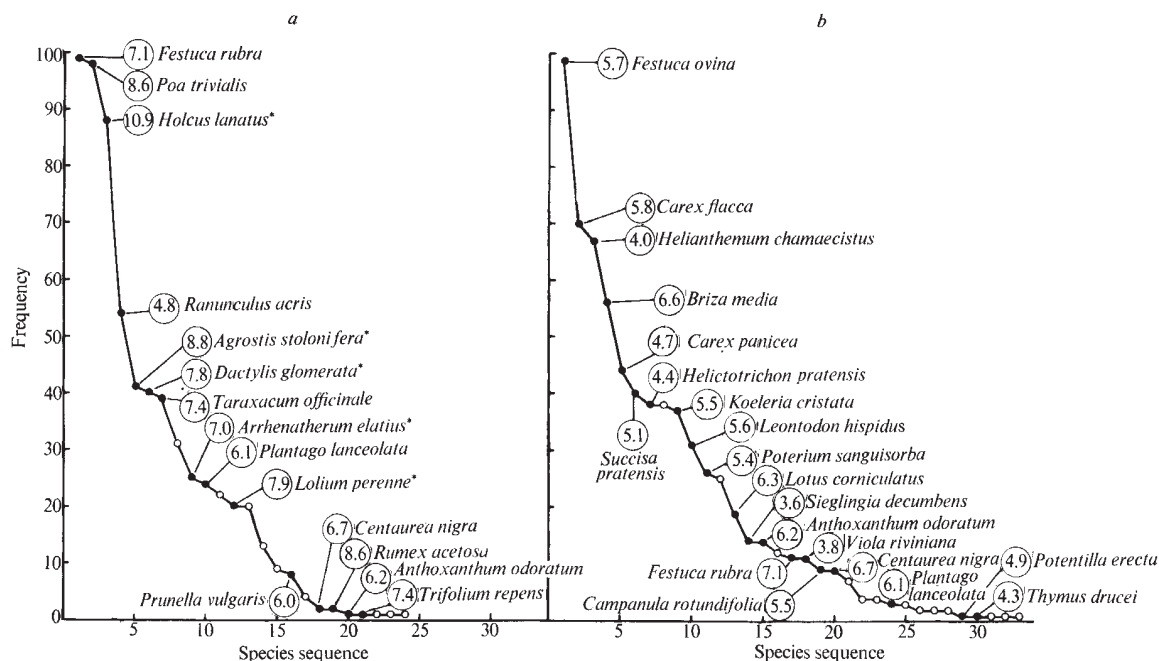


Fig. 5 Comparison of two m² samples of species-rich vegetation with respect to the potential growth rates of the component species. *a*, Productive meadow (Coombsdale, Derbyshire). *b*, Ancient limestone pasture (Cressbrookdale, Derbyshire). (Grime and Hunt, unpublished.) In each figure the species are arranged in order of decreasing % occurrence in 10 × 10 cm subdivisions of the m² quadrat. The encircled values refer to the RGR_{max} of the species. The open circles indicate species for which no growth-rate estimations are available. * Species of high (>6.0) competitive index.

species density when grazing or mowing is relaxed. Where values for RGR_{max} are low the ensuing reduction in species density is likely to proceed at a relatively slow rate.

Here differences in species density have been related to variation in stress imposed by environment or by certain forms of management and to variation in the frequency and vigour of species of high competitive ability. The impact of additional factors such as site accessibility and degree of niche-differentiation upon species density will be reported elsewhere.

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Gestation Period for Australopithecus

LEUTENEGGER¹ has provided estimates of the foetal size at birth of two species of *Australopithecus*. Huggett and Widdas² drew attention to the relationship between foetal age and weight in mammals, and we have been assessing both specific foetal growth rates and length of gestation (J. F. D. F. and A. St G. Huggett, unpublished data). It is quite clear that in the higher primates the foetal growth rate is 0.06. Using this and the estimates of foetal sizes at birth in the Huggett/Widdas formula² we obtain gestation periods for *A. africanus* of 257 days and *A. robustus* 300 days.

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Measurement of the Diffusion Coefficient in the Concentrated Phases of the Soap-Water System by Nuclear Magnetic Resonance

A MEASUREMENT of the lateral diffusion coefficient of spin labels in lecithin bilayers has been reported by McConnell *et al.*¹ This diffusion is found to be rapid, the consequences of which, in terms of the structure of biological membranes, cannot be overlooked. Here we report the result of nuclear magnetic resonance measurements on the diffusion coefficient in the concentrated phases of the potassium laurate-heavy water system. Our results strengthen the theory that diffusion in lipid water systems is rapid, magnetic resonance measurements have the advantage that it is the diffusion of the constituent molecule itself that is being observed and not the diffusion of an added "impurity" as is the case with spin label experiments.

The usual procedure for measuring diffusion by magnetic resonance is to observe the decay of the spin echo in the pulse sequence $90^\circ, \tau, 180^\circ$ as a function of τ , or as a function of the applied magnetic field gradient. This method is valid only for the inequality $12/\gamma^2 G^2 D \leq T_2^2$ being satisfied where γ is the magneto-gyric ratio of the resonant nuclei, G is the applied magnetic field gradient, D the self diffusion coefficient and T_2 the nuclear transverse relaxation time. This condition is normally satisfied for liquids of low viscosity where the diffusion is fairly rapid and the transverse relaxation time T_2 is of the order of the longitudinal relaxation time T_1 . In the concentrated phases of amphiphile-water systems the T_2 is normally too short, owing to dipole-dipole interactions, for a liquid echo, and hence a diffusion coefficient to be obtained by this method. One method of overcoming this difficulty is measurement of the stimulated echo, first described by Hahn² and further developed for diffusion measurements by Tanner³.

To obtain a stimulated echo a sequence of three 90° pulses is required. The echo which occurs an interval after the third r.f. pulse equal to that between the first two pulses is unique in that its relaxation attenuation has a T_1 dependence as a function of the interval between the second and third r.f. pulses. The attenuation of the stimulated echo in this case is given by

$$\ln(M/M_0) = -\frac{(\tau_2 - \tau_1)}{T_1} - 2\frac{\tau_1}{T_2} - \ln 2 - \gamma^2 D g \tau_1^2 (\tau_2 - \tau_1/3)$$

where M_0 and M are the nuclear signal initially and at the time of the echo maximum respectively, τ_1 and τ_2 are the time intervals between the first and second, and first and third r.f. pulses. An additional condition discussed by Tanner³ for optimizing the three 90° pulse sequence for minimum non-diffusional attenuation at fixed diffusional attenuation is that $\tau_2/\tau_1 = T_1/T_2$; also, as the attenuation depends on τ_1^2 , this quantity cannot be made too small and in practice must remain a few milliseconds. Thus if the ratio of T_1/T_2 is large, the interval τ_2 must be large and this can cause problems of signal to noise ratio and often, as in our case, demand that signal accumulation and averaging techniques be used.

The results on the potassium laurate-heavy water system prove interesting. In this system, X-ray work⁴ has shown the existence of a cubic phase. This phase is unique in that the absorption lines are so narrow that the spectrum can be studied by high resolution n.m.r. The spectrum is in fact very similar to that obtained in the micellar phase. This liquid-like behaviour is due to the complete averaging of the static dipolar interactions. Thus in this phase a liquid echo may be obtained by the sequence $90^\circ, 180^\circ$ and a diffusion constant measured. This has been

done by Charvolin (J. Charvolin and P. Rigny, to be published) who finds a diffusion coefficient at 80°C of $2 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$. Charvolin discusses the possibility of fast diffusion in the other concentrated phases. Here we have by means of the stimulated echo technique been able to measure directly the diffusion coefficient in both the hexagonal and the lamellar phases of the potassium laurate system. The results are a self diffusion coefficient of $2.3 (\pm 0.3) \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ in the hexagonal phase and $2.4 (\pm 0.35) \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ in the lamellar phase at 80°C . Concentrations were in the hexagonal phase 50% D_2O , and in the lamellar phase 28% D_2O . The temperature of 80°C was chosen because it is above the Krafft point for all phases. On decreasing the soap concentration and passing into the micellar solution, where a liquid echo is observed, the diffusion coefficient rises as a function of decreasing concentration. A factor 3 difference was observed in the diffusion coefficient at 12 g l^{-1} and at 120 g l^{-1} . This is to be expected, for what is now being observed is the diffusion of the micelles themselves becoming more rapid than that of their constituent molecules. A decrease is also observed in the activation energy from $5.7 (\pm 0.2) \text{ kcal mol}^{-1}$ at 120 g l^{-1} to $4.05 (\pm 0.1) \text{ kcal mol}^{-1}$ at 12 g l^{-1} . It is interesting to note that the activation energy in the cubic phase is $5.5 (\pm 0.2) \text{ kcal mol}^{-1}$ (J. C. and P. R., to be published) and in the hexagonal phase is $5.8 (\pm 0.2) \text{ kcal mol}^{-1}$. This tends to show that whatever macroscopic structure (hexagonal, cubic and so on) the molecular aggregations may take, the motion of the individual molecules remains very similar. We have also examined the diffusion of sodium lauryl sulphate in the hexagonal phase (50% D_2O) and found the extremely rapid diffusion coefficient of $1.6 (\pm 0.3) \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ at 88°C . An interesting point here which deserves further attention is that in the gel phase of the same concentration (that is at 25°C) the measured diffusion coefficient was $2.5 (\pm 0.4) \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$. This shows a factor 10 difference, and if one assumes a similar activation energy for the process (5 kcal mol^{-1}) then there must be an increase in mobility on passing into the hexagonal phase.

A model which could explain n.m.r. data is that of a molecule whose polar head is constrained to move only in two dimensions, but the terminal methyl group has a completely liquid-like character. Spin-diffusion is not an effective process along the hydrocarbon chain. The T_1 relaxation behaviour is governed primarily by rapid translational diffusion. A certain portion of the chain, however, near the polar head group remains relatively rigid; within this part of the chain, dipolar interactions exist. This gives rise to the T_2 mechanism and also the $T_{1\rho}$.

These results are extremely interesting especially for biological membranes. An ordered system that looks viscous is on the molecular scale behaving almost as a liquid. Examination of diffusion in cell membranes as regards function may throw considerable light on the transport properties.

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BOOK REVIEWS

Unmaking the Mess

The Spoils of Progress: Environmental Pollution in the Soviet Union. By Marshall I. Goldman. Pp. xi+372. (MIT Press: Cambridge, Massachusetts and London, 1972.) £3.60.

The Biology of Pollution. By Kenneth Mellanby. (The Institute of Biology's Study in Biology, No. 38.) Pp. 60. (Edward Arnold: London, November 1972.) £1.50 cloth; 75p paper.

Environment File. Prepared by Michael Hussey for the Technology Foundation Course Team. (The Open University: Bletchley, Bucks, 1972.)

THOSE of us who do not like regimentation often argue that if it were made easier for people to follow their own uncoerced preferences, many of the world's troubles would be ameliorated. It is argued that, if contraception were so perfect and universally accepted that the only babies born were those positively wanted, the population problem would disappear, and that if advertisers stopped foisting new wants on us, we would make much less mess. Goldman does not say anything about population, but he effectively demolishes the illusion that by abolishing advertising we would get rid of pollution. That leaves the abolition as a worthy cause in its own right.

Goldman is connected with the Russian Research Centre of Harvard and shows some sympathy with the initial objectives of the Russian revolution. His book is based on what he saw on many recent visits to the USSR and on intensive study of Russian newspapers and other publications. Although there is little advertising aimed simply at increasing consumption, Goldman makes it abundantly clear that the Russians nearly equal the Americans in their capacity to foul their environment. The main differences he notices are that the atmosphere is less fouled by lead from car exhausts, and there are few abandoned cars and refrigerators. As in other countries, there are laws prohibiting the discharge of noxious effluents, and, as in other countries, they are openly flouted. The Russian "remedy" is to pass a new set

of laws. He notes that Khrushchev introduced more of these laws than Lenin.

In spite of his sympathy with the revolution, Goldman sees ecological disadvantages in the monolithic state. To quote: "Instead of serving as a referee between polluters and conservationists, government officials usually support the polluters. It is necessary to remember that the state is the manufacturer . . .". Sometimes, however, pollution gets so bad that notice has to be taken of it. The result is a fine that can be as small as 5 roubles. To cover any inconvenience that might be caused by a larger fine, factory managers often include a sum to pay the fines in their financial plans at the beginning of the year.

The showpiece in this chamber of horrors is Lake Baikal. Because its water was once pure, a huge mill to produce very high quality paper was built there. It has now so fouled up the water that the site has lost its original merits. Many overlapping commissions were appointed to look into the matter and little attention was paid to their reports. Even the Central Committee of the Communist Party got involved in 1971. It would seem that the USSR has little to learn from Britain about the art of bamboozling the electorate. Russian officials, however, labour under one great disadvantage—the basic documents of their system condemn thoughtless exploitation. Goldman quotes Engels: "Thus at every step we are reminded that we by no means rule over nature like a conqueror . . . our mastery of it consists in the fact that we have the advantage over all other beings of being able to know and correctly apply its laws", and again: "Let us not, however, be very hopeful about our human conquest over nature. For each such victory, nature manages to take her revenge. Each of these victories, it is true, has a first order of consequences which we can anticipate. But in the second and third orders there are quite different, unforeseen effects . . .".

It seems from this book that, in the

USSR, fatheadedness and organizational momentum can do as much environmental damage as cupidity and a wasteful outlook do elsewhere. In Britain, projects such as urban motorways and Concorde get started and then acquire a life of their own that enables them to survive in spite of general disillusionment. According to Goldman, the Russian fetish is damming up rivers; he quotes the suggestion that the only reason for damming the Ili was that it was the only major river in Central Asia without a dam. Conservationists will join him in lamenting the gradual erosion of Russia's nature reserves. State ownership of land facilitated the establishment of an admirable system. As in other countries reserves have suffered from various forms of industrial encroachment: they have even become private hunting grounds for bureaucrats. But the picture is not unrelievedly black. Municipal central heating is spreading; there is consequently less atmospheric pollution. The area irrigated and fertilized with sewage is being rapidly extended.

The state of the law, and of its enforcement, is part of Mellanby's theme also. He explains that Common Law enables the owner of a stretch of river bank to proceed against anyone fouling his water, and that river authorities could, in theory, clean up the rivers if they moved against the 60 per cent of our urban population that is served by overloaded sewage works. He suggests that this would harm industry and cause unemployment. It is legitimate to wonder whether there would not be compensatory work in bringing the sewage works up to standard and in organizing efficient recycling processes. Mellanby lists some improvements—the Thames is cleaner than it was 20 years ago and smokeless zones make a difference that is obvious to the most casual observer. He deplores both uninformed alarm and uncritical complacency. Thus he urges those who stress only the harm that insecticides can do to consider also the need for them if crops are to be protected and diseases are to be

checked in countries less fortunate than Britain. And he points out that although the amount of lead, derived from doped petrol, absorbed by city-dwellers does not exceed the danger level set by the health authorities, that level may itself be criticizable.

The bundle of eight "exhibits" from the Open University is hard to assess. Some have merely an emotional impact; there is some useful information on the construction and consequences of the Aswan High Dam, and some gloomy forecasts of what will happen if everything goes on happening as it does now. The most valuable "exhibit" is the text of a lecture by Dubos in 1971; he argues that technology should be redirected towards meeting actual human needs, and points out the dangers in oversimplifying both ecosystems and problems.

For as long as an unpleasant state of affairs is regarded as "natural" there is little incentive to do anything about it. With the recognition that it is wholly or in part man-made comes the realization that it could be unmade. We must, therefore, welcome the intensity of discussion on such issues as pollution, ecology and population because, although much nonsense is talked, the fundamental point, that we made the mess and could unmake it, is winning acceptance. The next step, the decision whether the consequences of unmaking are worse than the mess, is more difficult.

N. W. PIRIE

Scientific Archaeology

Models in Archaeology. Edited by David L. Clarke. Pp. xxiv+1055. (Methuen: London, November 1972.) £16.

THE editor of this volume, David Clarke, is well known for his book *Analytical Archaeology* (reviewed in *Nature*, 220, 1357; 1968). This new book consists of twenty-six individual papers especially commissioned by him, each containing in its title the word "model". Together they are claimed to represent "the carefully selected work of progressive archaeologists around the world". The aim of most professional archaeologists today is to set their subject on a broadly scientific as distinct from an entirely subjective basis, and most of the authors in this volume are making a serious attempt to do this.

One possible approach is to tackle archaeological evidence by controlled quantification combined with structure-seeking computer programs. This is a rapidly developing field and relevant papers, for example by G. Cowgill on "Seriation", are serious contributions, although through time lag in publication, not perhaps in touch with the very latest developments. Two attempts to

incorporate such data analytic techniques into specific research projects are rather disappointing through misinterpretations of the published computer output: J. P. White and D. H. Thomas mistake the meaning of two of their three principal components for stone tools, through ignoring the equal importance of negative and positive loadings on such components; L. R. Binford chooses for rotation and interpretation five dimensions of a similar analysis when a simpler solution in two dimensions is indicated. These trivial but rather devastating slips could have been avoided by closer contact with relevant scientific colleagues.

Another related but more ambitious approach to archaeological data is represented by attempts to simulate by computer programming a past human society, so that given data may be replicated by suitable adjustment of the input to the artificial system. So far, no comprehensive results can be reported, but most interesting accounts of work in progress are given by J. E. Doran and D. H. Thomas.

In all of these papers, a "model" may be understood as a mathematical model providing a link between data and interpretation, where the fit of model to data may be specified and assessed. Most other papers interpret "modelling" more liberally. A major preoccupation is seen in locational studies, where geometric patterns are superimposed on known distributions of archaeological sites or features. The need here is to convince the reader that the chosen pattern fits the data better in shape and scale than other obvious patterns that could be tried. When there is no measure of fit, or a realistic null hypothesis (an assumed "random" scatter of points on irregular terrain is hardly a substitute for this), some readers will be less enthusiastic about this approach than others. A similar gap between reality and model is likely to occur when attempts are made to estimate the size of prehistoric populations by calculating quantities of food that could have been produced and consumed. The more cautious locational and demographic studies in the volume, however, are certainly among the most interesting.

Perhaps the least rewarding papers are those that militantly advocate a "new" as against a "traditional" archaeology. This represents a definite school (others have termed it a religion) which claims to have created a new scientific archaeology. Unfortunately, their creed does not depend on the inherent peculiarities and limitations of the relevant data, but on an uncritical allegiance to the tenets of selected philosophers of science. As might be expected, the result is a travesty of both science and archaeology, but it is maintained with

distinct fervour and is given more space and credence than it merits in this volume and elsewhere.

The high point of the volume is undoubtedly E. M. Jope's "Models in Medieval Studies", which demonstrates how many of the more serious techniques hailed currently by prehistorians as "new" have been exploited in a better documented branch of archaeology for decades. Only the jargon was missing. This Jope wittily provides and leaves the reader to ponder whether, after all, the real distinction in archaeology should be drawn not between a traditional and a new approach, but between good and bad scholarship.

F. R. HODSON

Nutritional Research

Malnutrition: Its Causation and Control. By John R. K. Robson. In Collaboration with Frances Larkin, Anita M. Sandretto and Bahram Tadayyon. Vol. 1. Pp. x+1-312. Vol. 2. Pp. x+313-613. (Gordon and Breach: London and New York, 1972.) £6.24 for two volumes.

Now that the clouds have lifted from the support of nutritional research, it is time that all the various items of knowledge in this large field were gathered together. This is exactly what these two volumes aim to do; and they succeed. The information is rightly carried into the socio-economic field. Again it is right that the books are dedicated to Professor B. S. Platt. The authors state that they have been "for 18 years engaged in the planning of nutrition programmes at national and local levels and the delivery of nutrition services in the richest and poorest countries of the world". The books cover laboratory as well as field research and teaching. It is accurate for the authors to describe nutrition as based upon "pure, applied and social sciences, including chemistry, biology, physiology, medicine, agriculture, education, sociology, economics, anthropology and politics". So often this is not realized.

In volume 1, the first long chapter deals with global nutrition, the effects of various deficiencies, including trace elements and protein-calorie deficiency, as well as overnutrition. This is followed by a more detailed chapter on the ecology and aetiology of malnutrition, dealing, among other things, with flour, rice, maize, the Irish potato problem and the size of families and weaning. The rest of volume 1 includes a chapter on normal nutrition giving the reader a condensed, but adequate, account of the physiology of the gastrointestinal tract and up to date knowledge of the biochemistry of the cell. In this, attention is given to transport systems, ATP, carbohydrates, fats, pro-

teins and their balance, nitrogen and energy balance, inherited disease, respiratory quotients, calorimetry and the action of vitamins. Useful summary diagrams are included. A valuable feature of both books is the set of references at the end of each chapter.

The second volume starts with a summary chapter on nutrient requirements; pains are taken to explain the different possible meanings of this, and the differences between the minimum and optimum requirements. Attention is given to recommendations of different bodies such as WHO and national schedules. A table gives recommended daily intake of vitamins, iron and protein at different ages. There is valuable critical discussion of tissue depletion, vitamin C and the increased need by elderly folk for thiamin, and the interaction of fats in the absorption of vitamin A.

Chapter 5, running to 108 pages, is occupied with the problem of the assessment of nutritional status, and is in some ways the most important, for the reason that a description is given in critical detail of the various possible approaches and the difficulties under field conditions of arriving at a true assessment. Its wisdom is clearly based upon much practical experience and should be read by anyone who thinks of starting such work. Part 2 concludes with a description of nutrition programmes and service, including problems of education. There is also a fascinating account of food habits, from which most would learn something which they do not know. I noticed with interest that there is no explanation of the replacement of calories by joules; surely it is better not to worry the reader with this new term in place of the universally accepted "calorie".

RUDOLPH PETERS

Mathematical Men

Men and Discoveries in Mathematics. By Bryan Morgan. Pp. xii + 235 + 9 photographs. (John Murray: London, October 1972.) £2.

MORGAN surveys the development of mathematics from antiquity to our times in a style suitable for the layman. Many such books are available now, and they should give this one a rough time, for they normally recount the same material with greater command and accuracy. For example, consider chapters 6 ("The Great All Rounder", referring to Gauss—although the last third deals with other mathematicians) and 7 ("Yesterday and Today"). Among the anachronisms, Gauss's contemporary Babbage is in chapter 7, and is falsely said to be "fifteen years later" than de Morgan; Weierstrass is in chapter 6, before Abel and Galois; and Fourier is a chapter early, in chapter 5.

There are also frequent errors of fact or questionable interpretation. In particular, in one section Morgan misrepresents Cantor's continuum hypothesis and claims that Cantor proved it, asserts that Kronecker's criticisms drove Cantor into a mental hospital, confuses Russell's *The Principles of Mathematics* with *Principia Mathematica*, describes Frege's *Die Grundgesetze der Arithmetik* as dealing with "the logic of classes", asserts that Russell tried to prove consistency, and identifies Gödel only as "an Austrian logician".

It is not worth going on; better to pick up the danger signals at the beginning. For anyone who thinks that M. Cantor's *Geschichte der Mathematik* is "definitive" and E. T. Bell's *Men of Mathematics* is "scholarly" must have a measure of historical command which is "there but not there", to use Morgan's misrepresentation elsewhere of Leibniz's infinitesimals.

I. GRATTAN-GUINNESS

Uses of Groups

The Fascination of Groups. By F. J. Budden. Pp. xviii + 596. (Cambridge University: London, August 1972.) £6; \$18.50.

THE basic reason for teaching any branch of mathematics to non-specialists is that it provides an appropriate language in which to talk about some interesting and frequently occurring class of phenomena. What that class is, in the case of well established branches, is something that we learn so early that we hardly think about it at all. Even the least numerate person knows that numbers are there for counting and measuring, and has some idea of the situations in which counting and measuring are useful. But with a less traditional subject, such as group theory, the kinds of situation in which the language applies, as well as the truths that can be expressed in it, have to be taught consciously. This is what is meant, in this context, by that rather misleading word motivation. The great merit of this book is that it makes a serious attempt to provide motivation in this sense; no one will learn much group theory from it, but anyone who reads it carefully will end up with some idea of what group theory is about. I doubt Mr Budden's claim that his book will be of use to university students, but I would expect it to be indispensable to teachers of mathematics in schools, and of immense value in school libraries.

What the book does first is to take the two ingredients of a group, a set and a binary operation on it, and the four conditions imposed on them, the

closure and associativity of the operation, and the existence of a neutral element and of inverses, and to examine them in turn, with a wealth of examples, chosen to show what the definitions exclude as well as what they include. The same detailed treatment is then given to such basic concepts as the order of an element, isomorphism, subgroups, direct products, and homomorphisms, and to the simplest classes of groups, cyclic groups and dihedral groups. Finally, there are four chapters on applications, to music, to bellringing, in geometry, and to plane symmetries. The chapter on applications to music includes an interesting example of motivation; namely, the relation between equally tempered and natural scales. One can think of the natural scales as reality: equal temperament is a mathematical construct, which simplifies reality at the cost of some distortion, and the simplification consists in this, that the set of intervals is now closed under the appropriate composition, and so forms a group.

I found the book irritating in places. Why, for example, should two successive chapters be labelled "Cyclic Groups" and "The Dihedral Group" when it is clear that on any interpretation there are just as many dihedral groups as cyclic ones? More seriously, it is a pity to state on page 410 that Galois proved that the alternating group A_n is simple for $n \geq 5$, and to suggest on page 411 that we do not know whether there is an infinity of finite simple groups. Again, it is perfectly reasonable to ask the reader to show that the relation $r^4=1$ is a consequence of the relations $ar=r^3a$ and $a^2=r^2$, but, for the sort of reader at which it is aimed, it seems too hard to be asked to prove that $r^4=1$ and $ar=r^3a$ do not imply $a^2=r^2$. At the very least, he should be asked first to consider carefully what sort of argument could possibly prove such a non-implication.

But these are minor blemishes. The book's only major blemish is its price.

GRAHAM HIGMAN

Echinoderms

Physiology of Echinoderms. By John Binyon. Pp. x + 264. (Pergamon: Oxford and New York, October 1972.) £4.80.

THE current spreading of interest in echinoderms, together with the physiological emphasis of many undergraduate courses in zoology, has created a need for an up-to-date review of the subject. The various chapters cover most aspects of echinoderm physiology, and Dr Binyon has used his knowledge and experience to provide a direct account of the topic.

The chapters on excretion, osmoregulation, biochemical affinities and respiratory physiology give useful surveys, but others are not so up to date. Important work has been carried out on feeding, digestion, chemical composition, toxins, sensory physiology, the excitable tissues, the water-vascular system and on spawning and neurosecretion which is not treated by the text. Of the references cited there, less than 5 per cent concern papers published after 1966, the date of the previous review of the subject. The author has provided an addendum of about 250 references, mostly to work carried out between 1966 and 1970, but these are not dealt with by the text so they merely direct the reader to possible sources of information.

Echinoderms constitute a singular group of animals, and many aspects of their biology are unique. Consequently the book would have been improved by the inclusion of an adequate introductory chapter. Readers not familiar with the phylum may have some difficulty with unexplained terminology, and little guidance is given on the organization and classification of the group. Although the author stresses that the unusual symmetry and the absence of a head have influenced the development of certain physiological systems, he might have emphasized other significant features that echinoderms display. These include the exclusively marine habit, the large coelom and the unique skeleton.

The usefulness of the book could have been increased if it had been planned differently. As it is, some information that would be of use earlier in the text is withheld until later and the headings and cross references do not always lead one to the expected information.

While this book will be valuable for some aspects of undergraduate work, it will be of limited assistance to the researcher because it is out of date in several respects.

ANDREW C. CAMPBELL

Viruses of Man

Strains of Human Viruses. Edited by M. Majer and S. A. Plotkin. Pp. x+271. (S. Karger: Basel and London, 1972.)

THIS book fulfils a long standing need in virology. Edited by M. Majer and S. A. Plotkin, with individual chapters contributed by different workers, it is a catalogue of the strains of human viruses which are either official prototype strains or which have been widely used by workers in the fields involved. Strains used for vaccines and those with genetic markers are also listed. In each

case, the source of the original isolate and the laboratory where the first isolation was made are given together with the passage history and a summary of the characteristic features of the strain. No book, of course, is perfect, and it is a real pity that in most instances there is no mention of the laboratories from which the viruses may be obtained. References to the literature on each strain are given which the editors suggest should be consulted for this information, but this is much less useful than a list of laboratories which stock the strain concerned. The editors also make apologies to "the scientist whose pet strain has been omitted" and there are certainly a few surprising omissions some of which will no doubt be corrected in a second edition. A more serious criticism is that in the chapter on herpes simplex virus it is not always stated if the strain is type 1 or type 2. In cases in which serological typing has not been done this should have been stated—although it is doubtful if such a strain merits inclusion at all. These criticisms, however, are minor and do not seriously detract from an exceptionally useful book. It will undoubtedly become an indispensable reference book in all virus laboratories.

MORAG C. TIMBURY

Plant Hormones

Plant Hormone Research in India. By S. M. Sircar. Pp. vi+264. (Indian Council of Agricultural Research: India, New Delhi, 1972.) Rs. 12.50.

THIS is a comprehensive volume, divided into three parts. The first provides a general account of plant hormones including historical aspects, terminology, chemistry, methods of application and mode of action. The second part is concerned mainly with the practical uses of hormones and, in addition to well known applications such as rooting, fruit setting and weed control, the effects of hormones on plant metabolism and their role in promoting growth of plant tissues and organs in sterile culture media are discussed. An account is also given of hormone inhibitors and growth retardants. In the third part of the book the author considers the potentials of growth hormone research. There is a chapter dealing with hormones in tropical plants in which particular attention is given to the results of Indian workers. The final chapter considers the importance of hormones in bud, stem, and fruit growth, abscission of leaves and fruit, and senescence.

Apart from the special attention given to Indian plants there is nothing very novel about this book. However, it is

quite well produced, with useful photographs, diagrams and an extensive bibliography and it has brought together most of the important findings of hormone research. Because of its special emphasis on local plants and crops it will be especially useful to botanical and agricultural students in India.

R. L. WAIN

Pictures of Rocks

The Minor Structures of Deformed Rocks: a Photographic Atlas. By L. E. Weiss. Pp. vii+431. (203 plates.) (Springer: Berlin and New York, 1972.) 94 DM; \$29.80.

THIS unusual book, which has been described as an atlas, contains more than 200 full or half-page plates with brief paragraphs, stating the types of structures, rocks and localities illustrated; a brief six-page introduction is followed by a further twelve pages, entitled "Introduction to Plates", two pages of references and a short subject index completes the text.

The author states that the main aim of the book is merely to illustrate the common minor structures resulting from rock deformation. The interpretation of such structures is left to other texts. For my part, I cannot agree with the author when he asserts that most field geologists are not and should not be concerned with the mechanical problems of rock flow. I believe that most people only "see" those things they understand, or think they understand. To this end I would have liked to see more interpretation in this book.

This apart, the book stands or falls on the coverage of material and the standard of photographic reproduction. The work contains about fifty plates illustrating planar features, more than seventy on folds and almost eighty further plates dealing with lineations, boudinage, veins and "complex" structures. The author freely admits that these structures represent his main interests and he has made no effort to include coverage of faults and joints, an omission which I find regrettable. The quality of the photographic content, which is due wholly to the author, and of the reproduction, ranges from acceptable to excellent, with a preponderance of the latter.

This work will doubtless be used by students as a "photographic" dictionary—a form of Duden—and, in addition, I am sure that teachers of structural geology around the world will contravene the laws of copyright and reproduce many of the plates presented, to augment their own teaching material.

NEVILLE J. PRICE

Primate Atlas

Taxonomic Atlas of Living Primates. By A. B. Chiarelli. Pp. vii+363. (Academic: New York and London, August 1972.) £6; \$18.50.

THE principal features of this atlas are an identification key and a series of species profiles providing information on distribution, body weight and size, coat coloration, synonyms and vernacular names. Most profiles have accompanying photographs and combined distribution maps are included. Attractive though this schema might appear to be, its realization sadly leaves much to be desired.

The basic classification itself would find few adherents today. Recognizing only suborders, families, genera and species, the author has his first suborder Prosimii embrace Tupaiidae and Tarsiidae as families of equal rank to five loriform and lemuriform families. At lower levels the general absence of subgenera and species groups, combined with some tendency to "lump", has meant the virtual disappearance of certain significant distinctions (for example, *Miopithecus*) and indications of special affinity (for example, among *Presbytis* species).

The identification key, while useful, is not without errors and its effectiveness is curtailed where, in spite of the claim to be based upon readily recognizable external features only, it relies on a knowledge of dental characteristics, the pelage colour of the neonate or the animal's provenance.

In the profiles of the individual species carelessness is everywhere apparent: mistakes and inconsistencies abound, and the brevity of treatment is such as to make many statements positively misleading. Weights and linear measurements are given without reference to sample size so that a range may in fact derive from only two animals, and a single figure may be either an average or a measurement from a single individual. Neither here nor elsewhere is there any indication of the extent to which subspecific variation occurs and affects the issue.

The descriptions of coat colour repeatedly fail to characterize adequately the species and the sections dealing with geographical distribution are no more satisfactory. Why are some ranges specified precisely but others given only in general terms? More disturbing is the frequency of errors in distribution data in both text and maps; examples are species of the genera *Tupaia*, *Papio*, *Presbytis*, *Colobus* and *Hylobates*, but many more could be cited.

Finally, too many photographs are of unnecessarily poor quality and line drawings have been used in some instances when very good photographs

exist. And the last thing one expects in a taxonomic atlas is the incorrect identification of photographs, yet this fault appears at least twice: the picture presented as *Tupaia ellioti* is not of that form (*Anathana*) but probably shows a southern *T. glis*; the so-called *Microcebus murinus* is really an infant *Galago senegalensis*.

One must conclude that although this work does serve a useful function even as it stands, it would have been so much better had more care been taken in its compilation.

G. H. MANLEY

Reproduction

Reproductive Patterns. Edited by C. R. Austin and R. V. Short. (*Reproduction in Mammals, Book 4.*) Pp. vii+156. (Cambridge University Press: London, 1972.) £3.40; \$11.95.

Artificial Control of Reproduction. Edited by C. R. Austin and R. V. Short. (*Reproduction in Mammals, Book 5.*) Pp. 152. (Cambridge University Press: London, 1972.) £3.40; \$11.95.

SCIENCE is usually written about either in a formal style by academics or in a more racy and provocative style by journalists. These two volumes, concluding the series *Reproduction in Mammals*, follow their predecessors in combining many of the attributes of both. Written by acknowledged experts in a lively and immensely readable fashion they cannot possibly fail to fan the interest of anyone with the least spark of curiosity about reproductive biology. The various authors have extracted their information from reliable and comprehensive sources, including their own contributions, and presented it in an uncluttered form with clarity and coherence. The numerous tables, graphs and line drawings have generally been used to good effect. In the many instances where different topics overlap there is a reference to other chapters in the series, and a sensible short reading list is given at the end of each chapter. The editors' brief was clearly to consider the human angle wherever possible, and this has been done by reference to known facts, and also by extrapolation and prognostication.

The authors have stood back from the trees and shown us what the wood really looks like. This is an ideal approach for newcomers to the subject, as well as for their teachers, and also serves as a useful compass for those who may have got lost in the depths. In the absence of any serious competition at this level of analysis these volumes are to be welcomed as a valuable addition to the teaching texts. And even student grants would run to the paperback issues. In some ways the

whole series might have been better published as a single volume, but this is a purely personal view.

The volume on reproductive patterns is not so restricted as the title might suggest, and as well as articles on species variation, environmental control and behaviour, there is consideration of immunological factors and of ageing. The whole is illustrative of the diversity of control processes in reproduction both within the individual and the society.

In the final volume stress is laid upon the pressing dual requirements for increasing farm animal production whilst severely limiting human reproductive potential. Hopes for the former are high, but there appears to be much less optimism for a significant assault on the latter. In all likelihood we shall have to rely on the perfection and application of presently available methods of contraception rather than hope for the development of any totally new ones, at least for a solution to the problem in the foreseeable future. The female of our species will be particularly dismayed to learn that there is no immediate prospect for a chemical method of male contraception.

It is often forgotten that for the individual problems of infertility and developmental abnormality are considered more urgent and distressing. The achievements and aspirations in these areas are also dealt with in this volume.

The series editors themselves conclude with frank discussions of the social, ethical and legal implications of manipulating human reproduction. Their stand is uncompromising. The present situation demands that we alter those attitudes that have been forged by cultural and religious dogma and assume full responsibility for the exploitation of new scientific techniques.

W. D. BILLINGTON

Finches of Europe

Finches. By I. Newton. Pp. 288+28 plates. (William Collins: London, February 1973.) £3.

THIS is an excellent account of the European representatives of an interesting group of small, stout-billed, seed-eating and often brightly coloured birds—the true finches (Fringillidae). There are two subfamilies, one comprising only the chaffinch, the brambling and a single extralimital form; the other, the cardueline finches, has well over a hundred species, of which sixteen are European. Much of the book is based on Dr Newton's own researches, but he has also made full use of the extensive literature.

Three chapters are devoted to a summary review of the eighteen species. Most of the others deal more generally

with different aspects of finch biology, taking examples from here and there and comparing one species with another. This is a valuable presentation, much that is said having a wider application than merely to the particular group. Geographical distribution and habitat preferences provide one aspect, and it is interesting to note the changes that have taken place in recent years in adaptation to the effects of human activities on the environment.

Feeding ecology is rightly given a prominent place. No two species of European finch have identical feeding habits; they differ in the sizes of seeds that they prefer and in the types of seed-head that they can best exploit, and these are related to the precise structure of the bill and to the particular method of using it. Nevertheless, new feeding habits can arise and spread through the population. The special feeding habits of the bullfinch have made it a major pest in orchard areas.

Further chapters deal with social behaviour, breeding, moult, migration and irruptions, and body weight. We are given an able statement of modern views on migration, applicable not only to these birds but largely to "hardy" migrants in general. Those finches that depend on the seeds of a few tree species, as contrasted with those dependent on herbaceous plants, show great differences in their movements from year to year in relation to a sporadic food-supply. The crossbills are a special case, moving only once a year and taking up new breeding areas.

The book is well illustrated with colour plates, photographs, drawings and clear maps and diagrams.

A. LANDSBOROUGH THOMSON

Heathland Microcosm

Ecology of Heathlands. By C. H. Gimingham. Pp. xv+266. (Chapman and Hall: London, October 1972.) £4.75.

As Professor Gimingham explains in his introduction, he has concentrated on certain aspects of the heathland ecosystem, in particular the vegetational components, but the lack of a detailed zoological treatment should not deter any ecologist interested in this subject. He has presented heathland as a microcosm. This feature alone makes his book different from the many ecological texts which rely on disparate examples: he is able to illustrate the whole range of plant ecology by reference to this particular vegetation type.

The characteristics of the plant, in particular its mode of growth, are shown to determine the nature of heathland and are related to such features as the current pattern in the vegetation, both short-term and longer-term history,

management practices, as well as the responses of the larger animals and even the physiological behaviour of the heather plant.

This dynamic interrelationship is a refreshing change. Recently the sledgehammer of numerical techniques has flattened the descriptive part of ecology; Professor Gimingham shows us what has been lost. In particular the chapters on growth form in relation to community structure, cyclical processes, management by fire and for grazing, nutrient cycling and conservation, make fascinating reading and exemplify this dynamic approach to the system.

I have only a few minor criticisms of this book. There is the usual crop of misprints, particularly in tables, and an unfortunate transposition of lines on the inside flap of the dustjacket—the part that most people will read first. In the chapter dealing with the phytosociology of heathlands, the reader might be forgiven for gaining the impression that, except for communities dominated by tree heaths, the southern limit of heathland is France. Many of the heath types (for example, *Calluna-Ulex* heaths, *Erica vagans* heath, humid heath with *Erica ciliaris*) all extend into the north and west of the Iberian peninsula; in fact, some of these have their phytogeographical centres in northern Spain. I should also have liked to see an expansion of the chapter on physiological ecology, perhaps particularly with regard to recent work on the photosynthetic behaviour of heather, although I must admit that this probably reflects only my personal bias.

In conclusion, I warmly recommend this book, not only to students of heathland, but also to anyone interested in ecology. It is a masterly analysis and exposition of ecology as the science of interactions.

P. BANNISTER

Has Man a Future?

Conservation for Survival: An Ecological Strategy. By Kai Curry-Lindahl. Pp. xiv+335. (Victor Gollancz: London, October 1972.) £3.25.

THE author of this book is a well-known Swedish zoologist who has taken an active part in international conservation activities, particularly in Europe and Africa. He has now taken a very broad and penetrating look at the world's problems and finds few crumbs of comfort in a long catalogue of man's folly. The first chapter is a global sketch of man's place in the world and his impact on the environment; chapters 2-8 consider the "Air", "Sea", "Fresh Water", "Soil", "Vegetation", "Animals", and "Man", while the last four discuss "Is Conservation a Losing Battle?", "Continental Problems of Today", "The Future" and "An Ecological

Strategy". Dr Curry-Lindahl's treatment of these subjects is probably more comprehensive than previous books of this type and the layman, for whom it was written, might find that there is too much for his mental digestion while any particular section which interests him is likely to be too brief. There are, for instance, 126 separate headings in 312 pages allowing 2.4 pages per subject. The simplification of ecological phenomena, which is perhaps inevitable in a popular book, leads to over-optimism in some cases (the value of biological control and the use of natural herbivores in Africa in preference to domestic stock, as a source of protein) while, elsewhere, the accusation might be over-pessimism, for example the alleged inability of food supplies to increase as rapidly as the predicted population expansion. Nevertheless it would be wrong to dismiss this book as just another of the many which have appeared in recent years on the evils of overpopulation and consequent environmental degradation. The reader feels entirely sympathetic to the feeling and understanding displayed by the author as he presents his case and the constructive points which are made in the final chapters.

There would be much agreement, for instance, for the view that too many of the politicians, planners and economists, who make decisions affecting us all, behave as if the size of the GNP is the only thing which determines the quality of life and that the standard of living can only be measured in economic terms because "progress" is equated with technological advance which is motivated by profit. The author asks for the formulation by the UN of "a world policy of management and utilization of renewable natural resources". This, he says, should be drawn up by a council which would be the highest international scientific authority on the conservation of nature and environmental problems. These are brave words but the history of action by the UN in other matters makes the mind boggle at the scale and extent of world catastrophes which would be needed to overcome the natural inertia of this organization. It seems that men of power find the needs of tomorrow too difficult to solve and so fall back to the events of today because it is the only ground they have to stand on and yet are unaware that it is slipping away from under their feet.

The book is provided with a glossary and "select bibliography" which includes the major books consulted and a selection of publications which appeared after the completion of the text. The references to original papers consulted were deleted by the author from the bibliography, at the publisher's request, but no one seems to have noticed that they still remain in the text.

ERIC DUFFEY

CORRESPONDENCE

Extraterrestrial Intelligence

SIR,—Nobody, it is to be hoped, now believes that the question, how many angels could stand on the head of a pin, used to be a standard topic of debate among the Schoolmen. Tenth-rate philosophers, then as now, may, of course, have debated many senseless things; but to suppose that men of the calibre of Albertus Magnus or St Thomas Aquinas would have wasted their time on such nonsense is absurd.

Yet the Schoolmen at least had this much on which to go, if they ever did consider such a question: they knew that the angels existed—or, at least, they thought that they knew it. But what is to be made of it when, in these enlightened times, men discuss things in the existence of which they have no real reason to believe? I am thinking of discussions about civilizations, or intelligent beings, outside the Earth, as for example in Walker's recent article (*Nature*, **241**, 379; 1973).

There is not, I suggest, a single bit of evidence to show that there is any likelihood that such things exist. What do we know about the matter? In the Solar System, every piece of new evidence makes it seem less and less likely that there are living beings of any kind, let alone intelligent ones, outside the Earth. As for hypothetical systems associated with other stars, we know—nothing. That there are binary stars, the members not necessarily of equal brightness or temperature, we know. It is quite possible that, in some cases, one of the pair might be relatively cool and small; and there may be some observations to support such a notion. But observations from a distance on our own Sun, if precise enough, would show that Jupiter is here. From what we see of Jupiter and the other giant planets, it would seem that, if there are planets around other stars, the more likely they are to be detected the less likely they are to be suitable homes for living beings. And even if matters of size and temperature could be resolved, we are, needless to say, far from finding out anything about the chemical composition of such hypothetical planets. But the composition is crucial to their suitability as homes for living beings.

Besides, the supposition that there are such intelligent beings in such situations depends on the supposition that intelligence will, somehow, arise of its own accord. But in any such view there are extremely grave philosophical difficulties, as even Darwin admitted.

So why do we not, for the time being, put a little more imagination into our discussions of extraterrestrial civilizations—we have nothing else to put into them anyway—and call them science fiction? If, then, the day should come when we have some sober facts on which to go, we could begin to call the result sober science.

Yours faithfully,

H. L. ARMSTRONG

Department of Physics,
Queens University, Kingston, Ontario

Neolithic Garden of Eden

SIR,—Mr Macy asks why, if one assumes the concept of a creator, should one then accept the idea of "fixed laws", such as gravity (*Nature*, **242**, 73; 1973). In answer, I suggest that he reads what Whitehead, Collingwood, Butterfield and Hookyaas have to say about the influence of religion on the rise of modern science. They conclude that belief in the Christian doctrine of the creation of an orderly universe by a rational God helped provide a philosophical climate in which science could flourish. It gave Kepler, Newton and so on a basis for belief in the existence of "natural laws" for which they could therefore confidently search.

If I understand him correctly, Mr Macy then says that religious and scientific models of the universe are "contradictory". Surely the word he should have used is "complementary"? The aim of religion is to understand the meaning and purpose of the universe. The aim of science is to understand its mechanism. This is why those who try to build a world view on a purely scientific basis often conclude, as they logically must, that there is no meaning or purpose to the universe. This does not prove that there is no purpose to it, only that the concept of purpose is excluded from science by its terms of reference. The complementary, and compatible, nature of Christianity and science is shown by the fact that modern science rests on a philosophical basis borrowed from Christian theology. As Collingwood has said "The presuppositions that go to make up this Catholic Faith . . . have as a matter of historical fact been the main or fundamental presuppositions of natural science ever since"¹. The major points of conflict between Christian theology and science have been at points where the former had, unfortunately, been adulterated by Aristotelianism.

When Mr Macy says that the book of Genesis must be taken as poetical, I

presume that he is referring only to the creation story. From chapter 12 onwards the archaeologist Albright can say "But as a whole the picture in Genesis is historical"². Even if the creation story is poetry, that does not exclude it from having a factual basis. What impresses me about it is how well it agrees with the available evidence. This is even more remarkable when one compares it with the fantastic nature of the other extant creation stories from the Near East. The order of creation given in Genesis is in general accord with the fossil evidence. Pearce³ has pointed out that chapters 2–4 agree well with what we know about the rise of neolithic culture in the Near East. Thus Adam and his immediate descendants are presented as stone age people (the first use of bronze is noted some generations later, in chapter 4, verse 22) who were agriculturalists living in settled communities. The origin of this culture is given as the Garden of Eden. The geographical position given for the Garden puts it in the area from which neolithic culture spread into the Middle East and Europe. It seems to me that far from being something to be sneered at or ignored the early chapters of Genesis form a very remarkable document, both from a historical and religious point of view, and they deserve to be taken seriously.

Yours faithfully,

E. C. LUCAS

The Dyson Perrins Laboratory,
South Parks Road, Oxford OX1 3QY

¹ Collingwood, R. G., *Essays in Metaphysics*, 227 (Oxford University Press, Oxford, 1966).

² Albright, F. W., *The Biblical Period from Abraham to Ezra*, 5 (Harper and Row, New York, 1963).

³ Pearce, E. K. V., *Who Was Adam?* (Paternoster Press, Exeter, 1969).

Square Cylinder

SIR,—A "cylinder" of square cross section. So the Cambridge applied mathematicians and/or theoretical physicists¹ have squared the circle or have they ciced the cylinder?

This is a protest against the misuse of universally accepted terms. A cylinder is essentially circular and cannot have a square cross section in the sense used. The body was apparently a right prism of square cross section or in common terms a square bar.

Yours faithfully,

P. B. N. NUTTALL-SMITH

21 Hall Lane, Yateley,
Camberley, Surrey

¹ Mulhearn, P. J., *Nature Physical Science*, **241**, 165 (1973).

HeLa

SIR,—I was pleased to read J. Douglas's question, "Who was HeLa?" (*Nature*, 242, 144; 1973).

I came across a poem by Nancy L. Caroline called "To Helen Larson" (*Perspectives in Biology and Medicine*, 15, 1971). It ends:—

Then Helen Larson wed. Her groom
Was cancer. Soon she felt
Death stirring deep within her womb.
She never tried to be immortal. She
died

Respectably but in her dying
Quite untied the knot of sex and death
Her breath ceased

In the tomb
Unmindful that her womb persisted
separately.

To multiply is to divide
Spawning immortality.

Yours faithfully,

P. P. GIORGI

Medical Research Council
Demyelinating Diseases Unit,
Newcastle General Hospital,
Westgate Road,
Newcastle upon Tyne NE4 6BE

Sense on Pollution

SIR,—Bearing in mind your obviously very deeply felt and persistent opposition to all things environmental, I suppose one must excuse the inaccuracy of the underestimate of current public concern about the environment implicit in your editorial "Measured Sense on Pollution" (*Nature*, 241, 489; 1973). What is much less excusable, however, is your assertion that "it has long since become apparent that British government depart-

ments are well equipped to take environmental problems in their stride". Since I find it impossible to believe that you could be so naive as seriously to consider that the British government and its civil servants, highly competent and widely experienced though they indubitably are, are presently equipped to cope with the manifold current and future environmental problems associated with population growth, increasing usage of dwindling natural resources, pollution and the need for adequate food production, I am bound to deplore the cynicism of your statement.

I am inclined to suspect that your ostensible claim that the bureaucrats will see us through, come hell or high (dirty) water, is in reality a restatement of the irresponsible and untenable view that, no matter what problems science and technology confront us with, technology and science will come up with a solution, the problematical side-effects of which will be solved by science and technology...

Yours faithfully,

PETER FERDINANDO

202 Carlton Road,
Gidea Park,
Romford,
Essex

Announcements

International Meetings

April 4, Third Weizmann Institute Lecture on "Membranes, Natural and Man-made" (Weizmann Institute Foundation, Rex House, 4/12 Regent Street, London SW1).

April 15–19, Third Conference on Recent Advances in Bio-Medical Engineering (John D. Gasking, Dept of Pharmacology, The Medical College, St Bartholomew's Hospital, Charterhouse Square, London EC1).

Erratum

In the News and Views article "Infection in Pregnancy and Foetal Growth" (*Nature*, 241, 425; 1973) our correspondent regrets that the work of Coid and Ramsden (on page 460 of that issue) was incorrectly quoted. The last sentence in the first column should read "The ratio of serum albumin to $\alpha 1$ foetoprotein was lower in the newborn mice which were growth retarded . . .".

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No. 22: An Altitudinal Sequence of Soils in the Sutton-Howth Area of Co. Dublin. By B. O'Flynn and J. F. Collins. Pp. 315–330. 50p. Vol. 4, No. 23: The Life Cycles of Some Invertebrates in an Isothermic Stream in Western Ireland. By Edward Fahy. Pp. 331–342+plate 14. 50p. Vol. 4, No. 24: Palaeomagnetic Results from Irish Carboniferous and Triassic Rocks. By F. G. Mulder. Pp. 343–350. 50p. Vol. 4, No. 25: Growth Trends of Zircons from the Northern Part of the Leinster Granites. By L. N. Gupta. Pp. 351–370. 50p. Series B. Vol. 3, No. 10: Observations of Some Fusarium Populations in Co. Donegal Cat Soils. By M. J. Downes. Pp. 127–136. 30p. Vol. 3, No. 11: The Reclamation of Mountain Soils and Attendant Profile and Land-Use Changes. By Michael J. Conry. Pp. 137–158+plate 2. 75p. (Dublin: Royal Dublin Society, 1972.) [241]

University of Oxford. Schedules of Lectures Authorized by Boards of Faculties, Hilary Term 1973. (Lecture Lists Supplement (2) to *Oxford University Gazette*, Volume CIII.) (Oxford: The University, 1973.) 20p. [241]

Radiopharmaceuticals and Clinical Radiation Sources, 1973/4. Pp. 91. (Amersham: The Radiochemical Centre, 1973.) [261]

National Survey of Air Pollution, 1961–71. Vol. 2: South West Region; Wales Region; North West Region. (Warren Spring Laboratory, Department of Trade and Industry.) Pp. viii+198. (London: HMSO, 1972.) £3.50 net. [261]

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